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VOLUME 107 • NUMBER 1

July 1967

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The Medical Association's Dealings With Governmental Plans

JOHN G. MORRISON, M.D., *San Leandro*, PRESIDENT, CALIFORNIA MEDICAL ASSOCIATION

ONLY A FEW CALIFORNIA MEDICAL ASSOCIATION members experience the emotions of those of their colleagues who have stood before you, as I do now, about to assume the responsibility with which you will soon entrust me. Until this moment when your new Presidents enter the highest office in this large state medical association, we are inclined to be flattered by, and proud of, the honor you accord us, rather than fearful of the responsibility we must assume. Then, as the day gets closer, some of us begin to hope that with a little bit of luck, we may be impeached beforehand. But this day always does arrive—when we stand before you, and realize that this is the first time, of many during the coming year, when you will expect your President to live up to your trust . . . and by his words and actions to do you credit. I can only hope to fulfill your expectations, as those who have preceded me in this office, have done so well.

Happily, because of the clear policies and precepts of your former officers, the Council, its many committees, this House of Delegates, along with the efforts of an earnest and dedicated staff, the task is less formidable than it seems. In fact, I am proud to look back over the past few years and observe that we, as an organization, have quietly and efficiently achieved a veritable “revolution” in the practice of medicine.

To refresh your memory:

Just ten years ago in October, the California Public Assistance Medical Care Act became operative. It was an improvement, but let me remind you of some of the things that that law con-

tained. First, the doctor had to ask the Welfare Department for permission to treat a patient. Equally rigid, was the fee schedule (\$4 on the RVS, remember?) which was justified by the State on the ground that California Physicians' Service had an even lower schedule (The A schedule, remember?), which it sold to non-indigent patients. Also, you could treat patients in the office—but if they were really sick and needed a hospital bed, back to the County hospital they went . . . deprived of your services when they needed you most, and when you most wanted to care for them. Now, there is virtually no prior authorization, little or no fee schedule. You can put your indigent patient in hospital where you want to—and there is much more comprehensive coverage.

Look at Workmen's Compensation. Up until about ten years ago, CMA had had almost nothing to do with the Industrial Accident Commission, except to denounce it occasionally. And for 40 years or so, California workmen who were injured were treated by the cheapest medical care that could be bought. Recognition was finally achieved that injured workmen are not second-class citizens medically and when they were put on a par with the rest of the population, one result concomitant with better care was the upgrading of medical fees; another was the promise to work toward the elimination of the fee schedule entirely.

Even Medicare surprised us when we learned the government was going to trust us by purchasing medical care for social security recipients at our usual rates. True, there have been some administrative ineptitudes, but I think most of us have been pleasantly surprised by the absence of

Presented before the House of Delegates, California Medical Association, Los Angeles, 15 April 1967.

Reprint requests to: 333 Estadillo, San Leandro 94577.

interference and arbitrariness which has characterized the government's attitude toward the medical profession so far in the Medicare program.

I think most of you who have met and dealt with government people will agree that, with a few exceptions, they are reasonable people. They have a growing sensitivity to Medicine's traditions and its need for freedom and individuality. I think the American Medical Association achieved this, over the last ten or fifteen years, by its courageous negotiations, testimony, advertising and education, by its diligent and unrelenting opposition to the wide and wild variety of compulsory health care legislation with which it was confronted. The whole "usual and customary" concept in present government programs, together with the medical freedoms and prerogatives which are a matter of law, resulted from the AMA's opposition. If the AMA had been perfect, if it had made no mistakes, we would have perfect medicine, and a perfect Medicare Act. But no one is perfect.

If you will compare the newest of government medical programs with some older ones—and particularly those proposals modified by AMA and CMA involvement—you will note they are all better than we have seen expressed in past programs. They are easier on the patient, partly because they are easier on us. They are more generous for the patient, because they are more generous with us. They are more productive for the patient because they let us do more things in a larger variety of ways.

These improvements are not happening merely because people, and particularly government people are getting smarter. I think they are happening because doctors are getting smarter. They are happening because doctors are concentrating, in their medical organizations, their experience and their ability to converse and instruct in the fiscal, administrative and political problems of medicine. In other words, doctors are learning to use not only their medical knowledge, but their fiscal, administrative and political know-how.

Only 20 years ago, *all* of the involvement of our county medical societies, the California Medical Association and the American Medical Association was still the subject of considerable debate. Many highly-respected leaders of medicine deplored the involvement of their scientific societies in the world of politics, in the hurly-burly of the market-place, in the rough and tumble of the courts. For instance, we hated to think about mal-

practice problems. Those doctors who concerned themselves with malpractice and other growing doctor-problems of the time, impressed us even while we looked a bit askance at them.

Now our medical societies are helping us in dealing with insurance companies. They help us talk to attorneys, to labor, to government, to news media, pressure groups and others. They help us to establish a reasonable relationship, in which neither party is threatening and neither party is fearful. In short, they serve as preservers of our traditions and as an authority to which we can turn for assurance and help.

Medical associations should now become the specific ombudsman for physicians as they have long been the medical ombudsman for our patients.

Physicians more and more, with the complexities of legislation and medical civics, understand their own need for an organized protector—in which each regards his own interest as best served by that which he knows to be most advantageous for all. We must let it be known that the finest public service we can render our members is the service that enables them to practice medicine of the highest standards in accordance with their training, their character and their conscience. If the hard-working, dues-paying member understands this—perhaps we can find it easy to forgive him if he does not read his socio-economic mail, if he does not know what is in Public Law 89-239, or PL 89-749 or what the Hart Bill is all about.

We now face a new year in California Medical Association activity. A new Council, new officers, a new staff organization—all demand reappraisal, a consolidation, a new realistic involvement by the medical profession in the health care matters of the state. As a state organization, we have done admirably, but we are still learning, still gathering experience and, in some ways, only just beginning.

We face many problems in the coming months—and we must realize that there may be no solution for certain situations, but that there are partial solutions for all situations.

What do we face?

The implementation of the Comprehensive Planning amendments makes it mandatory that all county medical associations become familiar with this law, and the report on which it is based. A cooperative, voluntary planning-involvement of our profession with all interested segments of society at a local level is of utmost importance.

The Heart Disease, Cancer and Stroke law is in the planning phase, and local involvement is important to keep this program in its proper perspective.

As to state government, I believe the time is past when we can passively await a call from Sacramento for advice. I would submit that we must actively seek participation in decisions, particularly in regard to mental health and medical legislation of all kinds.

I hope we will actively seek participation of those physicians who are not currently members of our association, especially the educators, who have as great a stake in where we go as any of the rest of us.

We must make better use of the advances in data collecting and automation—so we may better serve the needs of the public and of our members. These—and many other problems we will face—and I expect this House of Delegates to bring forth exemplary solutions to them.

In our efforts to consolidate and evaluate during the coming year, and years, we must be careful of several attitudes:

We must be careful to stay close to our working membership. We must see to it that we, as delegates, councilors, officers and staff, understand the membership's needs. We must continually "test" what we are doing, organizationally, against their understanding of it, against their prejudices, against their enthusiasms. It is *our* responsibility to see that the membership *understands*. If they don't understand what we are doing, we should stop doing it until we have explained it to their

satisfaction. If some of our committees stray from the understanding, consent and interest of our members—impatience, divisiveness and unrest soon develop.

We must be careful not to see our problems in terms which are too academic and thereby seek to solve them with formulas, gimmicks and rigid rules. The practice of medicine is practical and pragmatic—we deal with facts, realistic situations, and human problems, no two of which are ever alike.

The rules of medicine are rules which demand that the doctor be guided by his own character, training, judgment and intelligence—and they urge him to use everything he finds available for the comfort and well-being of his patient. I hope that our committees, made up of practicing physicians who know their calling and their needs, will remember this. I hope they will listen to their own instincts and find their own practical solutions.

Finally, we must be sure that our true character as a professional association is understood and appreciated. The group whose understanding is most important to us is our own membership. They will understand us most rapidly if we find their needs and serve them as best we can. We cannot persuade them with words—they are too busy to read our pronouncements. But they will believe and appreciate what we do when our actions arise not from unreal problems and solutions which others propose for us, but from our understanding of medicine's principles and medicine's needs.

Let us continue to build on an already distinguished record.



Gonorrhea

The Office Management of Acute Infections

LEONARD DAVIS, M.D., *Richmond*

■ *Gonorrhea has recently increased to epidemic proportions and is poorly controlled. The principal causes are probably increasing resistance of *Neisseria gonorrhoeae* to penicillin, the difficulty of establishing the diagnosis and proving the cure in female patients and the inadequacy of resources devoted to the eradication of the disease by public health agencies.*

While examination of smears is adequate for diagnosis of the disease in males, in females cultures of vaginal exudate are necessary. Gonorrhea can usually be successfully treated with large doses of short-acting penicillins. Intramuscular administration of aqueous procaine penicillin will bring about cure in most cases. Female patients should have cultures for several weeks to make sure they are cured.

The physician should report all cases to the local health department so that contacts can be traced and treated.

OVER THE PAST DECADE reported gonorrhea in California increased from 16,021 cases in 1954 to 35,665 in 1964. The experience was similar throughout the nation and indeed in many parts of the world.² To date there are no signs of a reversal of this trend.

The reasons for this epidemic do not seem to be well understood, but related factors are the difficulty of diagnosing infections in females (probably the main reservoir of the disease) and of demonstrating cure by bacteriological techniques.³ Often in the clinic of the Berkeley City Health Department, females examined because of gonorrheal contact are found to be completely asymptomatic, yet a culture of vaginal exudate grows *Neisseria gonorrhoeae*. Rectal gonorrhea in males is also usually completely asymptomatic and is only detected by routine cultures. An occasional

male appears to be a urethral "carrier,"⁴ having very minor symptoms which one would be inclined to ignore, yet culture of material from the urethral meatus will grow the organism.

Other factors in the epidemic are that the gonococcus has an ability to mutate and to adapt to antibiotics; the incubation period is short and the disease is readily transmittable on mucous membrane contact; there is poor reporting of the disease by physicians; and in many health departments resources for doing the necessary contact tracing are inadequate. Moreover, so rapid have been the changes in therapy that many practitioners are confused about the correct procedure and are unaware of the concept of "epidemiological treatment."

Diagnosis

Typically in men the incubation period for gonorrhea is three to seven days and the first symptoms are dysuria and a thick pus-like urethral

This article was written when the author was Public Health Resident with California State Department of Public Health assigned to Berkeley City Health Department.

Submitted 13 July 1966.

Reprint requests to: 185 Twenty-fifth Street, Richmond 94804.

discharge. On occasions, symptoms may be much milder and the discharge may be scant. It is desirable to confirm the clinical impression by examination of a smear. A methylene blue smear is easily prepared and examined in the office as described later.

A word of caution: It is easy to diagnose typical male gonococcal urethritis but the less typical cases should not be dismissed as nonspecific urethritis unless a properly taken culture shows no growth of the organism.

In the case of male homosexuals or women who have had rectal exposure, a culture is taken of material obtained by introducing the swab into the anal canal.

For males with a typical urethral discharge, smears alone will suffice to determine the diagnosis, and cultures are not necessary. However, in the case of a male with symptoms so slight that the diagnosis might well be nonspecific urethritis, a culture should be made. Cultures of material taken from the urethral meatus of the male will sometimes be positive even though no discharge is visible.

In summary, gonorrhea in males can be confirmed by smears but should not be excluded without cultures.

In women, acute gonorrhea may be completely asymptomatic or the patient may complain of urinary symptoms, vaginal discharge or lower abdominal pains. The complications in women are extensive and may include the whole gamut of pelvic inflammatory disease.

Throughout the whole course of disease, diagnosis in women is difficult and demonstration of the gonococcus by laboratory methods is inconsistent. On physical examination, the finding of vaginal discharge is of very little help since clinically this cannot reliably be differentiated from discharge associated with trichomoniasis, moniliasis or nonspecific vaginitis. However, if pus is pressed out on stripping the urethra or involvement of Bartholin's gland is noted or pain is evoked on moving the cervix, gonorrhea should be suspected.

Smears of vaginal discharge are of no great help as the miscellany of organisms makes the identification of gonorrhea difficult. However, properly taken cultures are valuable.

Differentiation from Nonspecific Urethritis

Nonspecific urethritis is a symptom of many diseases, not a single disease entity. It may or may

not be associated with intercourse, and the incubation period is highly variable and usually prolonged, as distinguished from the usual two to three days for gonococcal urethritis in males. The discharge tends to be scant, white and mucoid. The smear shows miscellaneous organisms, on culture there is no growth of *Neisseria gonorrhoeae* and the response to treatment is disappointing.

Smears

A smear of the discharge should be lightly spread on a microscope slide.

If the specimen is examined in a well-equipped laboratory, it will be Gram-stained and the examiner will look for Gram-negative intracellular diplococci.

In the office, a smear can be prepared by placing a drop of methylene blue on the slide, immediately washing it off under the tap and drying the slide over a lamp. The specimen is then examined under the oil immersion lens, and the intracellular diplococci are easily seen. In the Berkeley clinic we have found methylene blue smears helpful in confirming the clinical impression of gonorrhea and in differentiating it from nonspecific urethritis. However, it should be recognized that this method is not completely specific, as it will not differentiate Gram-positive and Gram-negative organisms.

Cultures

Material for cultures must be collected with special equipment. For this purpose the State Department of Public Health laboratory provides special charcoal-impregnated swabs and mailing tubes of Stuart's transport medium, which is an anaerobic medium. Different laboratories throughout the state will provide slightly different kits.

It must be noted that specimens collected on an ordinary sterile swab and introduced into a dry sterile tube are not satisfactory.

In females, one culture should be taken from the cervical os and one from the urethra. Both swabs can be introduced into the same tube of transport medium.

Treatment

Antibiotics

A great deal of confusion surrounds the use of antibiotics because treatment has changed over the years.

When sulfonamides became available in the 1930's, the gonococcus was found to be susceptible and at first the results of treatment were good. However, within a few years many strains of gon-

ococcus developed resistance to the sulfa drugs. Today sulfonamides are not usually effective in the treatment of gonorrhea and use of them should be avoided.⁵

With the introduction of penicillin in the 1940's, a rather similar cycle of events occurred. At first very small amounts of penicillin killed almost all strains of gonococcus, but over the years many strains showed increasing resistance. However, this resistance to penicillin is relative: The gonococcus remains susceptible to penicillin in higher doses, and penicillin of the right type in the right dose continues to be the drug of choice for the treatment of gonorrhea.

The essential point is that the amount of penicillin required to cure gonorrhea has gradually increased over the years and many customary treatment schedules are no longer effective.⁵

Types of Penicillin

There is an unfortunate tendency to talk of penicillin as though it were a specific drug. It is not. There are many different types of penicillin with different pharmacological properties and different indications for use. The following three basic types of penicillin are used in venereal disease clinics.

Aqueous procaine penicillin G (APP.) A short-acting preparation which rapidly attains high levels in the blood and is eliminated from the body in about 24 hours.

Procaine penicillin G with 2 per cent aluminum monostearate (PAM.). This preparation is released into the bloodstream more slowly than APP, does not reach blood levels as high as those with APP and persists in the body for 24 to 72 hours.

Benzathine penicillin G. This is the longest acting of the penicillins. It is released slowly into the blood, the blood levels are relatively low and it persists in the body for about one month.³

Gonorrhea is best treated with high blood levels of penicillin, which need be present only for a short time. Hence APP or combinations of APP and PAM are suitable. APP alone in high doses is the best treatment for gonorrhea and it is particularly suitable for resistant cases.¹ The combination of APP and PAM is more likely to eradicate concurrently acquired syphilis and is, therefore, the logical choice for the routine treatment of gonorrhea.

In most venereal disease clinics benzathine penicillin is considered to be contraindicated in the

treatment of gonorrhea because the prolonged low level penicillinemia is conducive to the development of resistant gonococcal strains.⁵ It should never be used alone in the treatment of gonorrhea. Benzathine penicillin is, however, the drug of choice for the treatment of syphilis.

Recommended Treatment

In Berkeley City Health Department's Venereal Disease Clinic the following treatment has been used for some years with a low failure rate, probably 1 or 2 per cent.

FOR UNCOMPLICATED GONORRHEA

| | |
|-------------------------------|----------------------------------------------------------------|
| Male Urethritis | } APP* and PAM* 1.2 million units (MU) intramuscularly of each |
| Female Urethritis, Cervicitis | |
| Epidemiological Treatment of | |
| Female Contacts | |

The USPHS has recently been advocating the use of twice the above dose (namely 2.4 MU each of APP and PAM⁶). However, it is difficult to administer that much penicillin to a patient, and the cure rate with 1.2 MU of each intramuscularly appears to be continuing at a satisfactory level.

For Resistant Gonorrhea

Resistant gonorrhea should be treated by doubling the original dose of antibiotics. In the Berkeley clinic, the intramuscular dose is increased to 2.4 MU each of APP and PAM and this treatment is invariably successful. The treatment of the complications of gonorrhea such as pelvic inflammatory disease and septic arthritis is beyond the scope of this article, except to mention that treatment is individualized and large doses of short-acting penicillin are used.

Allergic Sensitivity to Penicillin

Patients who have allergic sensitivity to penicillin can be treated with tetracycline USP capsules: One gram to begin with, then 0.5 gram every six hours for four days (36 capsules).

Follow-up of the Female Gonorrhea Patient

After the initial treatment females should be seen weekly, cultures being made each time of material taken from the urethra and cervix until successive cultures show no growth of organisms. If cultures continue positive, either reinfection or resistant gonorrhea is the cause.

*APP=aqueous procaine penicillin G; PAM=procaine penicillin G with 2 per cent aluminum monostearate. These penicillins are commonly available as:

Aqueous Procaine Penicillin G—*Crysticillin*® (Squibb); *Wycillin*, (Wyeth); *Duracillin*® (Lilly); *Abbocillin*® (Abbott); *Biurnal-Penicillin*® (Upjohn).

Procaine Penicillin G with 2 per cent aluminum monostearate—*Crysticillin P.A.M.*® (Squibb); *Depo-penicillin*® (Upjohn); *Leptopen*® (Wyeth); *Duracillin-in-oil*® (Lilly).

Reinfection is treated with the same dosage as the original illness. Resistant gonorrhea is treated with double the original dose of antibiotics administered at one time. For the rare patient with repeatedly positive cultures, we have treated successfully with APP, 4.8 MU intramuscularly, repeated two days later.

In the female patient, proof of cure is difficult to obtain by laboratory methods, yet the inadequately treated female who becomes an asymptomatic carrier is a major factor in the spread of the disease. Hence, the patient should not be considered cured until two or three successive cultures have been negative.

Treatment of Nonspecific Urethritis

Prostatic massage is frequently employed in treatment of nonspecific urethritis although most textbooks hold it valueless as a therapeutic measure. Tetracycline is usually given in therapeutic doses. A mild discharge which clears spontaneously or after a few days of tetracycline, is probably of little consequence, but a more persistent discharge warrants referral to a urologist.⁴ Most nonspecific urethritis responds to a course of tetracycline USP 250 milligrams four times a day, for four to six days.

Epidemiological Treatment

Since gonorrhea in women is frequently asymptomatic and demonstration of the gonococcus by laboratory methods is inconsistent,⁵ the USPHS recommends treatment of any female who is identified as a contact of a male who has the disease. This "epidemiological treatment"—which is the same as for uncomplicated acute gonorrhea—is standard practice in most venereal disease clinics. The purpose is to eradicate the carrier state in the woman and to prevent the progression of illness.

Differentiation of Reinfection and Drug Resistance

If gonorrheal reinfection is suspected, it should be treated as a new case. On the other hand, if drug resistance is suspected, double the original dose of antibiotics should be given at one time. The differentiation of these two conditions is based primarily on the history obtained from the patient and may well tax the physician's diagnostic acumen, not to speak of his credulity.

Concurrently Acquired Syphilis

Syphilis and gonorrhea are both transmitted by sexual intercourse and often a patient with

gonorrhea will have a positive reaction for syphilis by the Venereal Disease Research Laboratory (VDRL) test.

The dosages of aqueous procaine penicillin G and procaine penicillin G with 2 per cent aluminum monostearate recommended for gonorrhea will probably abort concurrently acquired syphilis. Nevertheless, any patient with a positive result of VDRL test (which is not reported until after the treatment for gonorrhea has been given) should be seen again and his condition assessed in the light of this new finding.

It should be borne in mind, however, that the recommended dosage of tetracycline for patients who have allergic sensitivity to penicillin is definitely inadequate to abort syphilis. Therefore, patients treated with tetracycline should have a serologic test for syphilis at the time of treatment and again several months later.

Reporting to the Health Department

Most males with gonorrhea will seek treatment for themselves, but their female contacts are usually unaware of the disease. Not only are they a reservoir for the spread of gonorrhea, but delay in treatment until they become symptomatic may well result in irreversible pathological changes. Similarly, the homosexual male with rectal gonorrhea is usually asymptomatic and constitutes another reservoir of the disease. Most health departments have trained venereal disease investigators who can help physicians to bring these contacts to treatment. California law requires that physicians report any cases of venereal disease to the local health department.

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Renal Disease Secondary to Metabolic Disorders or Physiological Deficiency States

RONALD OKUN, M.D., AND CHARLES R. KLEEMAN, M.D., *Los Angeles*

■ *Significant alterations in the structure and functions of the kidney are caused by a number of metabolic disturbances and deficiencies of physiological substances. These include intercapillary glomerulosclerosis, gout, hypercalcemia, hereditary cystinuria, potassium depletion, pyrophosphates deficiency, vitamin D deficiency and liver disorders. Some of these metabolic disorders are secondary to drug ingestion.*

SIGNIFICANT ALTERATIONS in the structure and function of the kidney are caused by a number of metabolic disturbances and deficiencies of physiological substances. In some of these conditions, the cause of renal derangement can be directly related to the metabolic disorder or deficiency state; in others, the association is significant statistically, but the causal relationship is less apparent. The most frequent and striking example of the latter is intercapillary glomerulosclerosis or Kimmelstiel-Wilson syndrome, associated with diabetes mellitus.

The intercapillary glomerulosclerosis of diabetes mellitus has at least two possible causes: (1) It may be a complication of the prolonged absolute or relative insulin deficiency and the resultant metabolic abnormalities, or (2) it may be due to an inherited susceptibility, operating concurrently with the metabolic defect, and progressing without regard to the degree of control of metabolic abnormalities. Unfortunately, diabetic glomerulosclerosis is rarely persistent alone; renal disease associated with diabetes mellitus usually

consists of glomerulosclerosis, severe hyaline arteriolosclerosis and focal or diffuse pyelonephritis. The clinical manifestations usually are determined by the predominant lesion. There is suggestive evidence that careful control of diabetes can minimize or postpone the development of clinically important renal disease.¹

Although nephropathy associated with diabetes can be suspected from certain laboratory evaluations (creatinine clearance, phenolsulfonphthalein excretion, urinary sediment examination, quantitative protein excretion and quantitative urine culture), a definitive diagnosis depends upon the results of histological examination of kidney tissue, usually obtained by needle biopsy. Intercapillary glomerulosclerosis is rarely the cause of the renal dysfunction in patients who do not have diabetic retinopathy (capillary microaneurysms).

There is no specific treatment for diabetic intercapillary glomerulosclerosis or the accompanying arteriolosclerosis. Treatment of urinary tract infection may be specific, but all other sequelae of renal dysfunction, which do not differ from those of other forms of renal failure with or without the nephrotic syndrome, must be treated symptomatically.

From the Division of Medicine, Cedars-Sinai Medical Center and the University of California School of Medicine, Los Angeles.
Submitted 27 October 1966.

Reprint requests to: Cedars-Sinai Medical Center, 8720 Beverly Boulevard, Los Angeles 90048 (Dr. Okun).

Although we doubt that there is anything characteristic about the type of diabetes mellitus associated with diabetic nephropathy, we believe that good control of the diabetes may decrease the renal morbidity.

The renal lesion associated with the *gouty trait* (hereditary or familial hyperuricemia) also is associated with three changes: Urate deposition in the medulla, severe arteriolosclerosis and focal or diffuse pyelonephritis. Evidence of renal disease is present in approximately 20 per cent of adults who have chronic hyperuricemia, regardless of whether overt attacks of gouty arthritis have occurred. In fact, severe renal failure may be seen in the complete absence of arthritis. The renal lesion appears to be more related to hyperuricemia than to excess excretion of uric acid. Most patients with the gouty trait do not have hyperuricosuria. The deposition of urate crystals in the medulla of the kidney is followed by fibrosis and tubular distortion, which predisposes the "gouty kidney" to urinary tract infection. Urate stones may or may not accompany the renal lesions.

Diagnosis of the gouty trait requires repeated demonstration of hyperuricemia when the patient is not taking drugs that lower the renal clearance of uric acid (for example, thiazides or aspirin). Percutaneous renal biopsy is seldom helpful in making a diagnosis of gouty nephropathy because the urate deposits in the medulla are rarely seen in the usual specimen. Treatment is aimed at reducing the uric acid level of the blood, which is accomplished by giving drugs (probenecid, sulfipyrazone) that increase the renal clearance of uric acid. When this treatment is begun, measures to assure a large volume of neutral or alkaline urine are essential. Alkaline potassium salts may be used rather than sodium bicarbonate when it is desirable not to give excess sodium. The thiazides may increase the concentration of uric acid in the blood by lowering its tubular secretion, and thus precipitate clinical gout and uric acid calculi. Potassium depletion *per se* may reduce the renal clearance of uric acid; therefore, a deficiency of this ion must be avoided when thiazides are given.

Any disorder causing hypercalcemia may be complicated by impairment of kidney function, ranging from a minimal defect in concentrating capacity to progressive renal failure. Deposition of calcium salts occurs mainly in the vessels, tubules and interstitial tissue of the renal medulla. In the earlier stages of impairment, degenerative and

necrotic alterations are apparent in the epithelium of the ascending loop of Henle, in the distal convoluted tubule and throughout the collecting system. Vascular disease and superimposed infection may play important contributory roles in the renal dysfunction associated with hypercalcemic nephropathy. One of the earliest signs is a diminished ability to concentrate the urine. Polyuria and polydipsia are often chief complaints. Rapid improvement in concentrating capacity frequently follows successful treatment of hypercalcemia. Proteinuria in hypercalcemic nephropathy is usually mild (less than 1.5 gm in 24 hours). The urinary sediment may be remarkably free of formed elements. Radiological evidence of stones or calcification of the kidney may be absent despite intensive nephrocalcinosis.

Treatment is aimed at the underlying cause of the hypercalcemia, but the degree to which impairment of renal function can be reversed is related to the extent of the scar formation, permanent medullary obstruction and infection, and to the presence of vascular disease. Even after hypercalcemia is relieved, renal function may remain depressed or deteriorate slowly, and occasionally it may improve. While hypercalciuria may be associated with nephrolithiasis, the hypercalcemia is the cause of the progressive nephrocalcinosis and renal failure.

In severe hereditary cystinuria a physiological disturbance causes the rate of cystine clearance to approach that of inulin. Cystine, which is poorly soluble in acidic urine, precipitates to form stones, and obstructive nephropathy may follow. Cystine also may form an insoluble complex with calcium. Treatment of this condition involves alkalization of the urine, large fluid intake, and low protein diets.

It has been suggested that certain physiological substances (pyrophosphates and phosphorus pentoxide compounds) capable of forming soluble complexes with calcium are present in lesser quantities in persons with stones than in those with normal urine. However, it is not possible at present to estimate the importance of these deficiencies and other factors favoring the solubility or insolubility of stone precursors.

It is now evident that chronic potassium depletion can alter seriously both the function and structure of the kidney.² Potassium depletion may result from excessive loss of fluid from the gastrointestinal tract (as from laxatives and enemas),

excessive use of diuretics, aldosterone-producing tumors, Cushing's syndrome and renal disorders such as tubular acidosis and Fanconi's syndrome.

Potassium is the principal intracellular cation and it has a vital role in maintenance of the normal cell. However, little can be said about the manner in which potassium deficiency causes widespread alterations in cell function and in the structure of the nephron. Nephropathy can be suspected in a person with a history of prolonged potassium depletion, evidence of a low serum potassium level (usually less than 3.0 mEq per liter), polyuria, polydipsia, inability to form acidic urine, and minimal azotemia. Unfortunately, there is no pathognomonic histological lesion observable in the kidney. There is little published information regarding the reversibility of potassium-depletion nephropathy in man. In some patients, however, serial renal biopsy studies have shown complete repair several months after potassium repletion.

Vitamin D deficiency can result in a nonspecific proximal tubular hypofunction and aminoaciduria. Therapy consists of administering large doses of vitamin D, and complete recovery of tubular function usually occurs after about one month of treatment.

Disorders of the liver may be associated with renal abnormalities. Liver damage induced experimentally by choline deficiency may be associated with severe degenerative and hemorrhagic changes in the kidney. Hemorrhage, potassium depletion, hypotensive drugs and sedatives may contribute to the progressive reduction in renal blood flow and glomerular filtration rate, and to the resultant azotemia, which may occur with hepatic failure; however, the basic cause of the renal damage is unknown. The appearance of renal damage in association with liver failure has an ominous prognosis. There is no known specific therapy.

Diabetes mellitus has occurred after prolonged use of thiazide diuretics and commonly after use of diazoxide, a nondiuretic thiazide. The diabetes in such cases appears to be clinically identical to

familial diabetes. However, there is not yet sufficient experience nor has enough time passed to evaluate the effect of this drug-induced diabetes on the kidney. There is no reason to believe the kidneys will be spared. The thiazides have also been associated with hyperuricemia. In fact, it appears that most, if not all, drugs which are organic acids will hinder the renal clearance of uric acid. This drug-induced hyperuricemia has been associated with clinical gout but the effect on renal tissue has not been reported. With more time and careful observations, it is very likely that renal damage characteristic of gouty nephropathy will be found. Although many drugs can raise the serum uric acid, the thiazides are most commonly implicated because they are used for long periods and the doses required to cause this adverse effect are relatively low.

Hypercalcemia is an uncommon adverse reaction to chronic usage of antacids. Although there is evidence that most, if not all, patients absorb some of the calcium carbonate antacid, only occasionally does significant hypercalcemia occur. It is likely that patients who have hypercalcemia from this cause absorb greater amounts of antacid or the antacid more efficiently complexes phosphate in the gut and thus promotes calcium absorption. When beginning patients on antacid therapy, it is wise to obtain a serum calcium determination about one week later. There is no doubt that significant renal disease can result from this drug-induced hypercalcemia.

It seems safe to conclude that other types of "toxic" nephropathy due to deficiency states or metabolic disorders will be revealed as understanding of the basic biochemical changes in disease increases.

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Intracardiac Shunt

Use of the Hydrogen-Sensitive Catheter to Clarify False Positive Diagnosis of Left-to-Right Shunt

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■ *The charts of 142 patients who had diagnostic right heart catheterization with conventional oximetry, oxygen content determinations and hydrogen electrode curve recording for left-to-right shunt were reviewed. A false positive diagnosis of surgical significance would have been made in nine patients if the hydrogen electrode had not been used. In addition, a diagnosis of left-to-right shunt could have been made at the wrong chamber level in three additional cases.*

INTRODUCTION of the hydrogen-sensitive electrode catheter by Clark and Barger in 1959 was a major advance in the detection of intracardiac shunts.⁴ Previous methods of study such as oxygen content determinations, oximetry and nitrous oxide techniques were time-consuming, requiring multiple blood specimens, and were associated with a disturbing incidence of false positive and false negative diagnosis. Several observers have reported on the usefulness of hydrogen curves in establishing the presence of left-to-right shunts when conventional methods were inconclusive.^{5,6,12} Shunts as small as 50 ml per minute are detectable by hydrogen study.²

Our interest in this subject concerns primarily the presence of false positive diagnosis of intracardiac shunts as established by standard methods of study. Dye dilution curves have been of value in clarifying this dilemma when the two-catheter technique is employed. However, dye curves require withdrawal of multiple specimens of blood

and the procedure is distinctly more complex than the recording of hydrogen curves.

For the past three and a half years in our laboratory hydrogen curves have been recorded routinely along with conventional right heart techniques. This communication is a report of our experience with cases in which a false diagnosis of intracardiac shunt would have been made had it been based on conventional blood analysis (oxygen content or double scale oximetry or both).

Methods

The charts of 142 patients who had conventional right heart catheterization at the San Diego County Heart Center were reviewed. All of them had combined oxygen content determination and/or double scale oximetry in conjunction with hydrogen curve recordings.* Blood specimens were drawn anaerobically from all heart chambers and analyzed according to the method of Van Slyke and Neal.¹¹ Duplicate readings with checks to within 0.2 volume per cent were required on all specimens. The average number of specimens was

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Submitted 6 February 1967.

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*U.S. Catheter Company—Platinum Electrode Catheter No. 353-PT.

TABLE 1.—*Clinical and Cardiac Catheterization Data in Nine*

| <i>Case No.</i> | <i>Clinical Findings</i> | <i>Electrocardiogram</i> | <i>Chest X-Ray</i> |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------|
| 1 | 9-year-old boy with heart murmur since infancy. Asymptomatic. Physical findings of slight right precordial bulge. Grade IV systolic ejection murmur 2nd left intercostal space with a thrill 2nd left intercostal space. 2nd sound in pulmonic area louder or equals 2nd sound aortic area. | Right ventricular hypertrophy. | Prominent pulmonary artery with normal lung vascularity. |
| 2 | 51-year-old woman with history of progressive dyspnea and cyanosis of hands and lips of 18 months' duration. Physical findings of a prominent jugular A wave, positive hepatojugular reflux, right ventricular lift, pulmonary closure tap, and murmur of tricuspid insufficiency. | Right ventricular hypertrophy, right atrial hypertrophy and myocardial ischemia. | Progressive cardiomegaly, full main pulmonary artery, diminished vascularity peripherally in lung fields. |
| 3 | 3-year-old boy with heart murmur since birth. Grade III pansystolic murmur lower left sternal border. | Normal. | Left ventricular dilatation. |
| 4 | 11-year-old boy with heart murmur detected on routine physical examination at age 10. Auscultation revealed in grade II systolic murmur at left sternal border at base of heart radiating to left infraclavicular area. | Normal. | Possible right heart enlargement with normal pulmonary vasculature. |
| 5 | 22-year-old woman with heart murmur detected on routine examination at age 20. Auscultation received a pansystolic murmur at left sternal border at apex radiating to left axilla. | Normal. | Normal. |
| 6 | 13-year-old boy with heart murmur detected at age 10 on routine physical examination. Auscultation revealed a grade III systolic ejection murmur at left sternal border at 3rd intercostal space with poor radiation to apex and base. | Normal. | Normal. |
| 7 | 20-year-old man with history of heart murmur since age 10. Physical examination revealed a slight pectus excavatum and a grade III high-pitched systolic murmur at the left sternal border with a fixed and split P2. | Incomplete right bundle branch block. | Increased pulmonary vasculature with intrinsic pulsation of the mid one-third of the right lung. |
| 8 | 20-year-old woman with heart murmur heard on routine physical examination. Auscultation revealed grade III systolic ejection murmur 2nd left intercostal space with a thrill and early systolic ejection click. | Right atrial and right ventricular hypertrophy. | Dilatation of the pulmonary artery. |
| 9 | 40-year-old man with history of closure of ventricular septal defect at age 28. Auscultation revealed widespread precordial systolic ejection murmur maximum at 3rd left intercostal space. A widely split P2 and a diastolic decrescendo murmur at left sternal border. | Right ventricular hypertrophy. | Right ventricular enlargement. |

†Oximetry and Van Slyke determinations on same specimen.

Abbreviations: SVC=superior vena cava; RA=right atrium; RV=right ventricle; PA=pulmonary artery.

TABLE 2.—*Data on Three Cases in Which Shunt Could Have Been Diagnos*

| <i>Case No.</i> | <i>Clinical Findings</i> | <i>Electrocardiogram</i> | <i>Chest X-Ray</i> |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|--------------------|
| 10 | 7-year-old boy with heart murmur since birth. Auscultation revealed grade III pansystolic murmur lower left sternal border with associated thrill. | Normal. | Normal. |
| 11 | 21-year-old man with heart murmur since infancy. Auscultation revealed grade II systolic murmur 2nd left intercostal space without a thrill. | Normal. | Normal. |
| 12 | 18-year-old boy with heart murmur since birth. Auscultation revealed an apical pansystolic murmur with thrill at the 3rd left intercostal space. | Normal. | Normal. |

*Proved at operation.

†Oximetry and Van Slyke determinations on same specimen.

Abbreviations: SVC=superior vena cava; RA=right atrium; RV=right ventricle; PA=pulmonary artery.

ses with Clear-Cut Step-up in Saturation or Oxygen Content

| <i>Hydrogen Data</i> | | | | <i>Catheterization Data</i> | | | | | | | | <i>Diagnosis</i> |
|----------------------|-----|-----|-----|------------------------------------|------|------|------|--------------------------------------|-------|-------|-------|----------------------------------------------------------------------------------------------------|
| SVC | RA | RV | PA | <i>†Oxygen Per Cent Saturation</i> | | | | <i>†Van Slyke in Volume Per Cent</i> | | | | |
| | | | | SVC | RA | RV | PA | SVC | RA | RV | PA | |
| Neg | Neg | Neg | Neg | 73.0 | 78.0 | 77.3 | 80.5 | 11.74 | 12.50 | 12.43 | 12.94 | Moderate pulmo- nary valve steno- sis with 38 mm Hg gradient. |
| Neg | Neg | Neg | Neg | 50.3 | 58.8 | 61.0 | 60.0 | 9.27 | 10.95 | 11.28 | 11.05 | Primary pulmo- nary hyperten- sion with pulmo- nary artery pres- sure of 100 mm Hg. |
| Neg | Neg | Neg | Neg | 73.8 | 75.6 | 81.7 | 79.0 | 10.38 | 10.60 | 11.55 | 11.20 | Minimal pulmo- nary stenosis with a 20 mm Hg gradient at pul- monic valve. |
| Neg | Neg | Neg | Neg | 70.0 | 75.4 | 75.0 | 80.0 | 11.70 | 12.60 | 12.60 | 13.35 | Minimal pulmo- nary stenosis with 20 mm Hg gradient at pul- monic valve. |
| Neg | Neg | Neg | Neg | 64.2 | 70.0 | 69.5 | 70.8 | 12.85 | 14.01 | 14.00 | 14.25 | Normal right heart study. |
| Neg | Neg | Neg | Neg | 65.2 | 73.2 | 70.5 | 70.9 | 11.30 | 12.75 | 12.30 | 12.38 | Minimal pulmo- nary stenosis with 20 mm Hg gradient at pul- monic valve. |
| Neg | Neg | Neg | Neg | 54.0 | 67.0 | 66.2 | 64.3 | 14.25 | 14.32 | 14.08 | 14.12 | Normal right heart study. |
| Neg | Neg | Neg | Neg | 60.8 | 66.0 | 67.0 | 68.0 | 13.99 | 14.88 | 15.15 | 15.20 | Moderate pulmo- nary valve steno- sis with a 73 mm Hg gradient at pulmonic valve. |
| Neg | Neg | Neg | Neg | 61.0 | 70.2 | 71.2 | 71.7 | 13.60 | 14.23 | 14.81 | 14.75 | Minimal pulmo- nary valve steno- sis with 25 mm Hg gradient at pulmonic valve. |

t Wrong Chamber Level Without Use of Hydrogen-Sensitive Catheter

| <i>Hydrogen Data</i> | | | | <i>Catheterization Data</i> | | | | | | | | <i>Diagnosis</i> |
|----------------------|-----|-----|-----|------------------------------------|------|------|------|--------------------------------------|-------|-------|-------|---------------------------------|
| SVC | RA | RV | PA | <i>†Oxygen Per Cent Saturation</i> | | | | <i>†Van Slyke in Volume Per Cent</i> | | | | |
| | | | | SVC | RA | RV | PA | SVC | RA | RV | PA | |
| Neg | Neg | Pos | Pos | 61.0 | 70.8 | 69.7 | 69.0 | 11.84 | 13.94 | 13.08 | 13.09 | Ventricular sep- tal defect. |
| Neg | Pos | Pos | Pos | 66.0 | 73.1 | 84.0 | 84.2 | 13.15 | 14.60 | 16.80 | 16.78 | Atrial septal defect.* |
| Neg | Neg | Pos | Pos | 62.5 | 83.1 | 81.8 | 81.0 | 10.53 | 14.68 | 13.61 | 13.65 | Ventricular sep- tal defect. |

13 per patient and they were drawn from the various right heart chambers, vena cava and main pulmonary artery. Double scale oximetry was performed by passing blood through a Waters Double Scale Oximeter Model X-70 A, readings being obtained during flow and no flow. Using this method, duplicate checks to within 1 per cent are obtained. A left-to-right shunt was considered to be present when a step-up of 1.5 volumes per cent occurred between superior vena cava and right atrium or 1.0 volumes per cent change between the right atrium and right ventricle or right ventricle and pulmonary artery. In a similar fashion an 8 per cent step-up on oximetry was considered compatible with a shunt at the atrial level, and a 5 per cent step-up was taken as evidence of a shunt at the ventricular or pulmonary artery levels.

Hydrogen curves were recorded in the main pulmonary artery, right ventricle, right atrium, superior vena cava and the innominate junction. Three curves were recorded at each site. Curves were recorded on a D.R.-8 recorder* with a paper speed of 25 mm per second. Inspiration was carefully noted on the record and the time interval from beginning of inspiration to deviation of the hydrogen curve from baseline was recorded. A left-to-right shunt was considered to be present when hydrogen curve deflection occurred in four seconds or less.

Results

In 22 of the 142 cases reviewed, the criteria for the presence of a left-to-right shunt were exceeded although hydrogen curves remained negative. Critical analysis of the 22 cases would permit exclusion of 10 cases on the basis of an isolated step-up not borne out on multiple specimens. In nine cases clear-cut step-up in saturation or in oxygen content were demonstrated on multiple samples in the face of negative hydrogen curves. It should also be noted that the clinical findings, electrocardiographic, phonocardiographic and radiographic features were also considered and supported the results obtained by hydrogen techniques in each case. Data on these cases are presented in Table 1.

In three cases positive hydrogen curves for a left-to-right shunt were confirmed by conventional technique, but in those three cases the shunt could have been diagnosed at the wrong chamber level

if only the conventional technique had been used (Table 2).

Discussion

The introduction of the platinum-tipped hydrogen-sensitive electrode by Clark and Barger on has constituted a major milestone in the study of intracardiac shunts. Previous reports^{7,8} have demonstrated the need for improved techniques in detecting left-to-right shunts and suggested the use of the nitrous oxide test. Still others advocated helium-oxygen,¹ krypton 85 inhalation test³ or the use of various indicator dilution curves¹⁰ as improved methods over the determination of oxygen content differences.

Hydrogen-sensitive electrode techniques have proved extremely reliable in the detection of extremely small shunts and the simplicity of the method makes it applicable in most cases. Vogel¹³ described a simplified bedside method for detecting intracardiac shunts utilizing an electrode catheter introduced percutaneously. Skelton and Corday⁹ also employed the hydrogen electrode for demonstrating aortic and tricuspid regurgitation. Our prime interest in reviewing this series was not to demonstrate its efficiency in clarifying the false negative studies obtained by oxygen content determination, but rather to point up its value in avoiding the false positive diagnosis sometimes reached by conventional studies. False positive diagnosis occurred in 8.4 percent of the cases reviewed, which could have resulted in needless operation or repeated catheterization because of variance with the clinical observations.

It is our belief that the hydrogen-sensitive electrode should be routinely included in right heart catheterization in any case in which there is even remote possibility of a left-to-right shunt.

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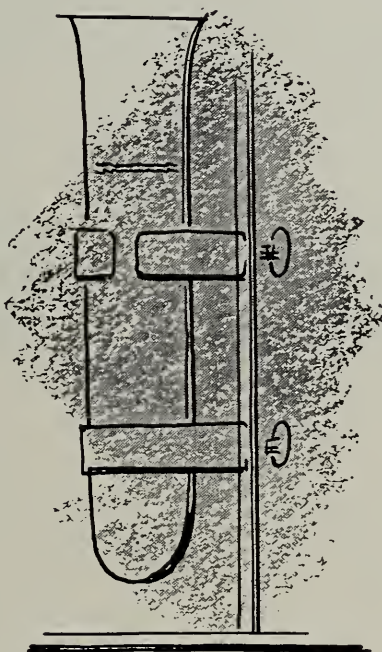
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Routine High Dose Excretory Urography

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■ *Radiologic evaluation of 316 excretory urograms utilizing a single 50 ml injection of a 50 to 60 per cent tri-iodinated contrast medium indicated that these studies are of better quality than those previously obtained with the injection of 30 ml. The low incidence of side effects coincides with recent reports in the literature that this dosage level is safe. High dose intravenous drip infusion pyelography was necessary only in selected cases. High dose excretory urography is recommended for routine use.*

SEVERAL INVESTIGATORS HAVE recently advocated higher doses of contrast medium for excretory urography.^{1,3,6,7} The use of higher dose techniques in children^{4,5} has already gained wide acceptance with pediatric radiologists. When the routine study with a 30-ml injection does not completely delineate the pelvocaliceal systems and ureters, other studies may be used, such as retrograde pyelography with its attendant surgical risk, and intravenous infusion pyelography.

Whether an additional 30 ml of contrast medium is injected 15 minutes after the initial injection,⁸ or a standard dose of 50 ml is used,¹ or a sliding scale of 30 to 100 ml depending on body surface area,² all investigators agree that radiographic visualization is improved with little if any increase in toxicity. Certainly, if the higher dose methods improve excretory pyelography without endangering the patient, and if procedures with higher morbidity are thus averted, high dose urography should be adopted. The clinical study here reported was carried out to determine whether the routine use of higher doses of contrast medium

improves the radiographic demonstration of the urinary tracts without increasing patient reactions.

Method and Materials

Since autumn 1965, 50 ml of contrast medium has been given to every adult patient and an occasional large adolescent referred for excretory urography to the Radiology Department of Children's Hospital in San Francisco. The first 56 patients received Hypaque® 50,† and the next 253 patients (with 260 examinations) received Renografin® 60.‡ All patients also received 10 mg of Chlortrimeton®§ mixed with the contrast medium. Ages ranged from 12 to 86 years, and weights from 85 to 295 pounds. Injection time was from 10 to 15 seconds in studies for hypertension and ranged upward to 1 to 2 minutes in other cases. All patients were observed in the immediate post-injection period by the administering physician and by the radiology technician until the patient left the Radiology Department. Side effects of nausea, vomiting, chills, itch and other significant reactions were recorded. Films were routinely taken at 5, 10, and 15 minutes after injection, with variations in time and position as indicated. A lower ab-

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Submitted 26 July 1966.

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†Sodium diatrizoate, Winthrop.

‡Methylglucamine diatrizoate, Squibb.

§Chlorpheniramine maleate, Schering.

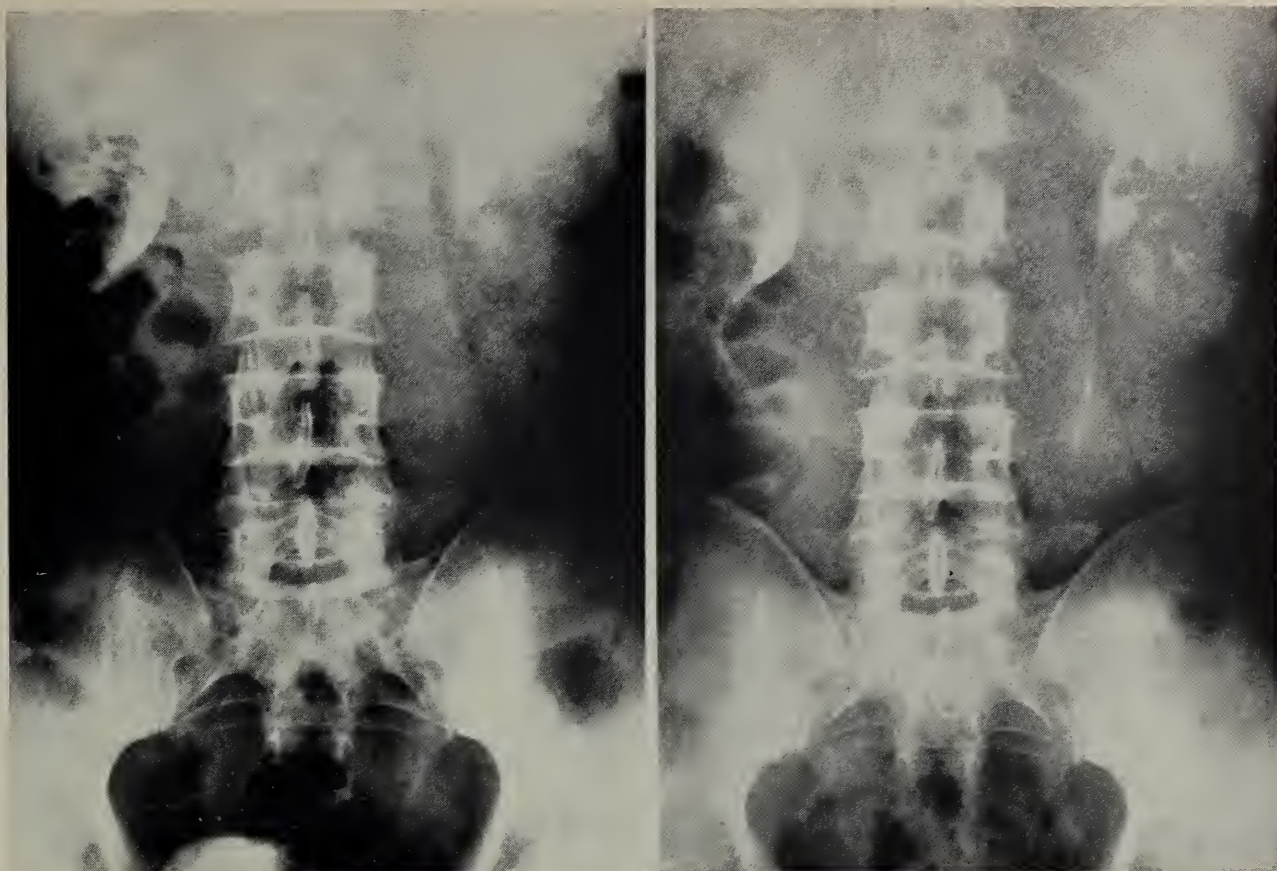


Figure 1A—Left, after injection of 30 ml of Hypaque® 50; right, after 50 ml of Renografin® 60. The preparation of the patient was essentially the same before both studies. The 50 ml study (1B) is considerably more “contrasty” and the pelvocaliceal systems more distended. The dilated right upper pole calyx from previous surgical operation that is revealed on the 50 ml study is unrecognized on the 30 ml study.

dominal compression was applied if there was no question of ureteral obstruction or abdominal-pelvic mass. This routine was similar to that previously used when 30 ml of contrast medium was injected. All studies were independently evaluated by two radiologists. Studies were graded as poor, fair, good or excellent. In addition, if previous studies with 30 ml had been done (in our department), and if the clinical situation was similar, the two studies were compared.

Serum creatinine* was studied in 47 patients in order to observe if poor radiographic visualization would be related to abnormal values. The blood specimen was obtained immediately preceding the injection of contrast medium.

Results

In a total of 316 separate studies in 309 patients, only one patient had more than minor side effects. He had had nausea and vomiting during a previous excretory urogram, and when given 1 ml of contrast medium for the most recent study,

conjunctival itch and engorgement, sneezing, nausea and vomiting developed. The injection of contrast medium was immediately discontinued and the symptoms abated without further complication. Three other patients experienced vomiting, nine had nausea alone, and one other patient had transient itch without rash. One patient who had a generalized rash following Telepaque®† given orally had no reaction to the Renografin® 60 while receiving steroid medication.

The radiographic evaluations of the 260 Renografin® 60 studies were as follows: 228 studies good or excellent, 26 studies fair (one of which improved to good with re-injection), five studies poor, and one study unsuccessful (this in the case of the patient who received only 1 ml of contrast because of a reaction).

Of the 47 patients on whom serum creatinine were studied, ten were found to have slightly elevated levels (1.4 to 1.8 mg per 100 ml) and nine others had higher levels. In none of these cases was the excretory urogram rated as poor.

*Method used at Children's Hospital and Adult Medical Center: Jaffe reaction—normal values 0.7-1.3 mg per 100 ml.

†Iopanoic acid, Winthrop.

Analyzing the group rated as fair, two of the patients had repeat examinations a few days later and the urograms were then rated good. Twenty-one of the 26 patients with "fair" urograms were either poorly prepared for the study or had clinical evidence of impaired renal function or urinary tract disease or hypertension. Studies that were rated fair in five other instances are not readily explainable. In the poor group (five patients), one had severe hypertension and obesity, one was hypertensive, one was azotemic, one had urinary tract disease and one had hyaline casts in the urine.

Fourteen patients weighing 195 pounds or more were examined. Ten of them had good to excellent examinations (including one woman of 295 pounds), three (with evidence of renal disease in two) had fair studies, and one (severely hypertensive) had a poor study.

Eleven studies were done on patients in whom the clinical conditions were essentially unchanged from those obtaining at the time of previous 30 ml studies. Nine of the eleven 50 ml studies were rated as superior to the 30 ml studies and two were similar.

Discussion

A scientific comparison of differing dose levels is not obtainable because of variation in kidney status in the same patient at different times (variations in preparation, hydration, technique and pathologic condition) and because of differences between patients. Furthermore, good objective criteria for comparing intravenous urograms are not available, and thus the appraisal of high dose studies as compared with routine dose studies will have to be made by the experienced radiologist. We feel that the higher dose technique results in a significantly improved study by virtue of better radiographic contrast of the urinary system (Figure 1) and the more complete filling of the pelvocaliceal system and ureters.

Many patients without evident disease of the urinary tract showed complete opacification of one or both ureters (Figure 2); therefore, complete ureteral filling previously considered as an indication of ureteral obstruction should be evaluated with slightly different radiologic criteria with high dose urography.

We believe that with the improvement in delineation of the urinary system, the need for retro-



Figure 2.—Five minute film, after 50 ml of Renografin® 60, without abdominal compression. Note the virtually complete filling of the ureters bilaterally in this normal study. With 50 ml of contrast medium, complete ureteral filling no longer necessarily indicates disease.

grade pyelograms with its risks will be further diminished.

It was necessary in only five cases to re-inject after giving an initial 50 ml. This is considerably lower than the need for re-injection using 30 ml in our experience. In one patient with azotemia and one with a large abdominal mass no improvement in visualization was noted with re-injection, but there was notable improvement in the case of one patient with hypertension and another with urinary tract disease. In one other case re-injection helped to determine more precisely the site of a urethral stone distal to a hydroureter and hydronephrosis.

The use of a graduated scale of 30 to 100 ml of contrast medium dependent upon body surface area² is felt to be unnecessary. Ten of the 14 patients over 190 pounds in the present study had good or excellent studies with only 50 ml, and all but one of the less satisfactory studies were readily explainable.

In this study, a slight elevation of serum creatinine did not seem to interfere with good radiographic visualization of the urinary tract.

Finally, the incidence of side effects in our study was low, but the number of cases was too small to

permit saying with certainty that the risk is not increased in comparison with 30 ml studies.

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Subphrenic Abscess

Roentgen Considerations

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■ *Roentgen findings in subphrenic abscess, in the order of their specificity and clinical value, are subphrenic air-fluid level, elevation and restriction of motion of the diaphragm, pleural reaction with congestion, segmental atelectasis or pneumonitis at the lung base and upper abdominal mass. Less frequently there may be empyema or bronchopleural fistula.*

Suppression of the infection by antibiotics may protract the course and obscure the clinical findings. Serial x-ray and fluoroscopic studies are recommended when a patient who has had rupture of a viscus or previous abdominal operation does not completely recover or has a persistent low-grade fever.

BEFORE THE ADVENT of antibiotics the development of a subphrenic abscess often followed a rather well defined course. With the masking or suppressive effect of antibiotics, there now may be a much longer interval between the exciting cause and the established diagnosis of abscess. It is important to realize that any patient who has had a ruptured viscus or abdominal operation (especially on the stomach or gallbladder) is a candidate for the development of a subphrenic abscess, particularly within the first six months. During this time, the clinical signs and symptoms may be non-specific or, as previously noted, masked by antibiotics. Roentgen examination and consultation are of value in suggesting or confirming the diagnosis.

In 154 cases of subphrenic abscess reported by Berens, Gray and Dockerty,¹ 40 per cent developed within one month of the exciting cause, 35 per cent between one and six months, 13 per cent between six and twelve months and 10 per cent after a year. There are other reports of delayed

diagnosis of abscesses as late as three years after the initiating lesion.⁴

In the acute cases which develop within a few days or weeks, the signs and symptoms are often clear-cut and the relationship to the source of infection obvious. However, in the subacute and chronic cases the symptoms may be mild—malaise, low-grade fever and pain in the chest, upper abdomen or back. Tenderness may develop over the liver, lower chest or upper abdomen. In some cases the primary complaints are referable to the lung. Twenty of 29 patients reported by Boyd² had pulmonary complications. The roentgen examination is particularly important in such patients. If the x-ray study is equivocal, serial films are indicated for observation of minor changes. Since all the roentgen signs of abscess are present in some cases while in others there may be only one or two positive findings, correlation with the clinical history and physical examination is essential. The x-ray findings vary with the size and location of the abscess; with small collections of pus there may be no positive findings or the changes may be so slight that they are not diagnostic.

Submitted 4 August 1966.

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X-ray Studies

The general condition of the patient may be such that examination must be limited, but when possible all patients with suspected abscesses should have:

- Postero-anterior and lateral films of the chest.
- Fluoroscopic examination of the diaphragm.
- X-ray study of the abdomen, supine position.
- X-ray study of the upper abdomen, erect and/or lateral decubitus.

In order of frequency in a series of 23 cases the positive signs were:

1. Progressive unilateral elevation of the diaphragm (or elevation of both leaves with bilateral subphrenic abscess).

Normally the right leaf of the diaphragm is slightly higher than the left, but in a small proportion of patients the two leaves are symmetrical, and in even fewer the left leaf is slightly higher.

Difficulties in interpretation arise in the immediate postoperative period when the diaphragm is usually slightly elevated and motion restricted, particularly following upper abdominal operations. Postoperative ileus or generalized peritonitis may also be associated with diaphragmatic elevation and restricted motion. Primary basilar pulmonary infiltration or atelectasis may be accompanied by slight elevation of the diaphragm. These other entities must be excluded clinically and radiologically.

2. *Restricted diaphragmatic excursion.* This is particularly important and is usually associated with elevation of the diaphragm. Fluoroscopy should be carried out in various degrees of rotation as there may be total or segmental restricted motion or lag as compared with the normal side.

With chest or abdominal pain from any cause, there may be transient limited mobility of the diaphragm. Often with basilar pulmonary lesions which may or may not be associated with the elevation of the diaphragm, there is limitation of diaphragmatic motion. Thus, restricted motion suggests the diagnosis only when associated with diaphragmatic elevation or suggestive clinical findings.

3. *Basilar pulmonary densities.* There is usually a basilar hypostasis associated with the elevated diaphragm secondary to abscess, and in addition many patients show segmental atelectasis or basilar pneumonitis. These changes are nonspecific and must be differentiated from infarct, pneumo-

nia, pneumonitis and congestive failure, any of which can be expected in postoperative patients or in those seriously ill from a ruptured viscus.

4. *Pleural effusion or empyema.* Effusion is a frequent roentgen finding in subphrenic abscess. It may develop concomitantly with the elevation of the diaphragm and basilar hypostasis, or it may be the initial roentgen change. A lateral decubitus film may be necessary to check the diaphragmatic level if the fluid obliterates its outline in the erect position.

Initially the effusion is sterile but later may become purulent, or the abscess may rupture through the diaphragm into the pleural space. A bronchopleural fistula may form. Carter and Brewer³ and Boyd² discussed the thoracic complications in detail.

5. *Extra-alimentary air below the diaphragm.* An air-fluid level below the diaphragm outside the alimentary tract is almost specific for abscess. Decubitus, erect and lateral films will outline the abscess cavity. Heavy density films are necessary when searching for a subphrenic abscess, for routine films often are too light to penetrate the liver density. All air shadows in the upper abdomen must be identified; this is particularly difficult in the left upper quadrant, owing to overlap of the stomach and bowel gas shadows. Interposition of the colon may be misinterpreted and it may be necessary to use opaque media to outline the stomach or bowel.

6. *Soft tissue mass.* A soft tissue mass may be contiguous with the liver, making the liver appear enlarged. On the left side the stomach or colon are often displaced by the abscess. In such cases barium studies may be helpful.

Any or all of the above roentgen findings will be present in a subphrenic abscess in contact with the diaphragm unless the lesion is early or small. At first there may be no roentgen findings but, as the lesion progresses, fluoroscopy and careful comparison of a series of films should show the first positive changes, such as slight elevation of the diaphragm, limited diaphragmatic excursion or a small pleural effusion.

With collection of pus in the liver, below the liver or even in the lesser sac, the roentgen findings are not as typical or as specific as when the abscess is in the immediate subphrenic region; a mass or air-fluid level may be demonstrated but the diaphragmatic and pulmonary changes are less frequent. Infection is rarely confined to one ana-

tomical area. Many abscesses are loculated, and thus persist after apparent drainage. In such cases it is most important to have serial films to detect minimal changes which indicate persistence or recrudescence of the lesion.

Case Findings

The present report is based on the x-ray studies of 23 patients with subphrenic abscess in contact with the diaphragm seen in the x-ray department of St. Joseph's Hospital in the last 20 years.

The abscesses developed chiefly in association with surgical operation as has been reported in previous series. In the 23 patients the causes were:

Surgical operation in 13 cases—Six gastric resections (one with rupture at the suture line and one in which splenectomy also was done); three colectomies, three cholecystectomies and one pancreatectomy.

Ruptured viscus in nine cases—Three duodenal ulcers, one sigmoid colon, three appendices and two gallbladders.

Source unknown, one case.

Thirteen abscesses were on the right, five on the left and five bilateral. The fact that the original disease was on the right did not exclude abscess on the left. One patient (case reported herein) had a ruptured appendix with bilateral abscesses, and one had a ruptured gallbladder with a left subphrenic abscess and a right subhepatic abscess. All patients in this report had surgical drainage, and in eight drainage was carried out more than once.

The interval between the initiating lesion in these patients and the first diagnosis of abscess was as follows:

In 13, diagnosis was made and drainage carried out initially in less than one month; and, of these—

One had residual abscess drained at one week;

One had recurrent abscess drained at one and a half and five weeks;

One had recurrent abscess drained at four months;

One had recurrent abscess drained at 15 months.

In nine, diagnosis was made and drainage carried out initially between one and two months; and of these—

One had a second abscess on the other side drained two weeks later and again one week later;

One had a recurrent abscess drained at one month;

One had residual or recurrent abscesses at five, nine and ten weeks and again at four and a half months;

In one, diagnosis was made and drainage carried out at eight months, with a residual abscess at one month.

Thus late development or recrudescence, over two months after diagnosis and initial treatment, occurred in six instances.

Three patients died with overwhelming infection—in one case after rupture of the appendix complicated by a lymphosarcoma of the small bowel and mesentery; in another after rupture of the gallbladder in an elderly patient in whom huge subphrenic and pelvic abscesses developed; and in the third when subphrenic abscess and then small bowel obstruction due to intraperitoneal abscesses, fistula and peritonitis developed after perforation of a sigmoid diverticulum.

The findings on the initial roentgen examination, before specific treatment, in the 23 patients were as follows:

| | No. of Cases |
|-----------------------------------------------|--------------|
| Elevated diaphragm | 18 |
| Limited motion or fixation of diaphragm..... | 16 |
| Air-fluid level below diaphragm..... | 14 |
| Pleural fluid | 12 |
| Soft tissue mass, abdomen, displacing viscera | 5 |
| Ileus | 2 |
| Lower border liver prominence..... | 1 |

Since the earliest clinical and roentgen changes are nonspecific, a definite diagnosis often could not be made until the signs were more advanced. When

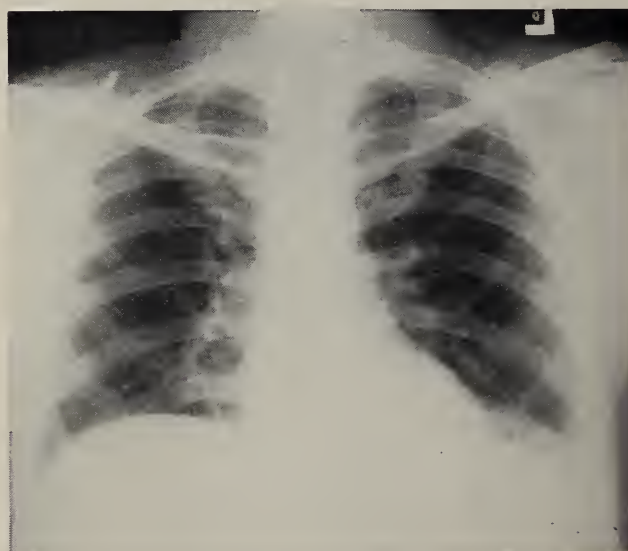


Figure 1.—Eight days after cholecystectomy. Good motion of right hemidiaphragm. Pleural reaction at the left base with slight limitation of motion on the left.

the abscess occurred or was reactivated there was recurrence or extension of these findings.

In the patients with abscesses developing soon after surgical operation or perforation, limitation of motion and elevation of the diaphragm was the initial finding, with basilar pneumonitis, congestion or fluid occurring later. Patients in whom the course of disease was protracted, however, uniformly showed not only the diaphragmatic and pulmonary changes but an air-fluid level below the diaphragm, and/or displacement of viscera due to the soft tissue mass.

The following three cases illustrate the clinical problems and roentgen findings.

CASE 1.—This case illustrates the protracted course with mild symptoms that may ensue when a subphrenic abscess develops while the patient is under medical treatment. The roentgenograms showed specific positive findings and indicated a positive diagnosis.

The patient, a man 40 years of age, was in good health until, three weeks before he was admitted to hospital, pain developed in the right upper quadrant of the abdomen and was accompanied by nausea and vomiting. Cholecystectomy and common duct exploration were done without difficulty.

The pathologist reported acute cholecystitis and cholelithiasis.

The patient went into shock 15 hours after operation and was treated with cortisone and antibiotics for a week. The temperature was 37.8 to

38.3°C (100 to 101°F) for a few days and then decreased to 37.0 to 37.8°C (98.6 to 100°F). There was slight pain in the left side of the chest. X-ray films on the eighth postoperative day (Figure 1) showed slight pleural reaction in the left costophrenic angle, good motion of the right hemidiaphragm and slight limitation on the left. T-tube cholangiograms were negative.

Malaise, anorexia and pain in the right side of the chest then developed. The temperature gradually rose with daily elevations to 38.3 to 38.9°C (101 to 102°F). X-ray studies two weeks after operation (Figure 2) showed slight hypostasis at the right lung base with an elevated, fixed right hemidiaphragm. The left costophrenic angle was clear. The diagnosis was right subphrenic abscess.

The right subphrenic space was opened and drained of 550 ml of blood and pus, a specimen of which grew *B. coli* on culture. Malaise, anorexia and irregular elevation of temperature persisted. Ten days later x-ray studies (Figure 3) showed the right hemidiaphragm to be 4 cm higher than the left with a large air-fluid level below it. There was basilar congestion and pleural reaction. Drainage was carried out and the patient was treated with antibiotics. X-ray films five weeks later (Figure 4), which was approximately two months after the initial operation, showed residual right basilar congestion with pleural reaction, and an elevated fixed right hemidiaphragm. The large right subphrenic abscess with fluid level was still

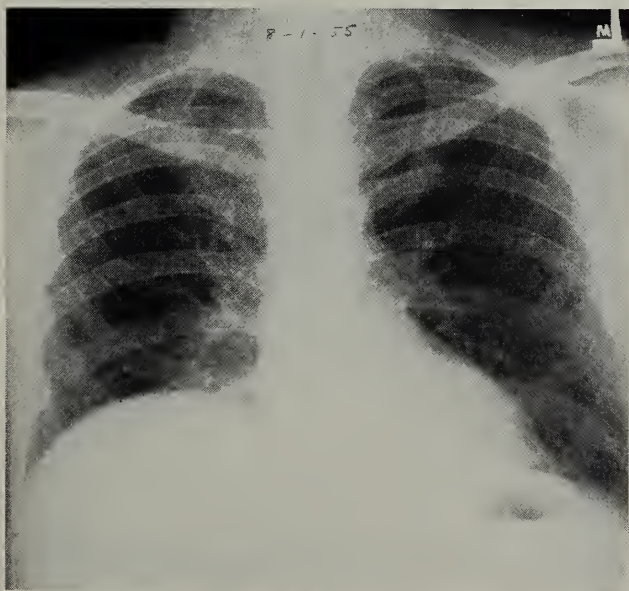


Figure 2.—Two weeks after operation. Right hemidiaphragm now fixed and elevated with right basilar congestion. Roentgen diagnosis: Subphrenic abscess.



Figure 3.—Ten days after drainage of the abscess, an air-fluid level shown below right hemidiaphragm. Note progressive congestion and reaction at the right lung base and hypostasis at the left base. The patient was treated with antibiotics and drainage was carried out.

evident. This was again opened and drained. The right pleural space was tapped and only sterile serous fluid obtained. The patient then improved slowly and was discharged, afebrile, two and one-half months after the initial operation.

CASE 2.—This case is of interest because of the initial clinical impression of pneumonia and empyema and the diagnosis of subphrenic abscess on roentgenographic findings.

The patient was a boy 10 years of age who, five weeks before the present admittance to hospital, had had drainage of a ruptured appendix. He did well for two weeks after the procedure, but then chills and sweats developed, with pain in the left side of the chest and temperature of 40.0°C (104°F). Films of the chest were reported to show left basilar pneumonia and the patient was treated with antibiotics without improvement. He entered the hospital with a clinical diagnosis of pneumonia and empyema. The temperature ranged from 38.3 to 39.4°C (101 to 103°F) and leukocytes numbered 15,000 to 23,000 cu mm of blood. Thoracentesis yielded 250 ml of clear sterile fluid and a repeat tap one week later was dry. At that time x-ray studies showed left basilar congestion and elevation of the left hemidiaphragm, which was fixed posteriorly. A large left subphrenic abscess with an air-fluid level indented the gastric fundus. The right hemidiaphragm moved and was at a normal level; the right lung base was clear. The left subphrenic space was drained and the temper-

ature promptly decreased and the patient's general condition improved.

Ten days later symptoms recurred. X-ray studies showed no pulmonary or pleural reaction. The left hemidiaphragm had little motion; the right was slightly elevated and there was limited motion. Four days later, right pleural effusion was observed, with an air-fluid level below the right hemidiaphragm. The right subphrenic space was drained of 400 ml of pus, and a week later drainage was carried out again. There was gradual improvement and the patient was discharged, in good condition, seven weeks after entering the hospital.

CASE 3.—This case is of particular interest because of the long interval, almost 15 months, between the initial subphrenic abscess and the diagnosis of recurrent indolent abscess. Also, as in Case 2, pneumonia was the clinical roentgenographic diagnosis on admission to hospital.

Fifteen months before the present admission to hospital, the patient, a 51-year-old man, had had subtotal gastric resection for chronic penetrating gastric ulcer. The postoperative course had been stormy, including drainage of a right subphrenic abscess 15 days after the procedure. He had recovered slowly, staying in the hospital three months. His body weight had decreased 60 pounds in that time.

After discharge he was able to return to work,

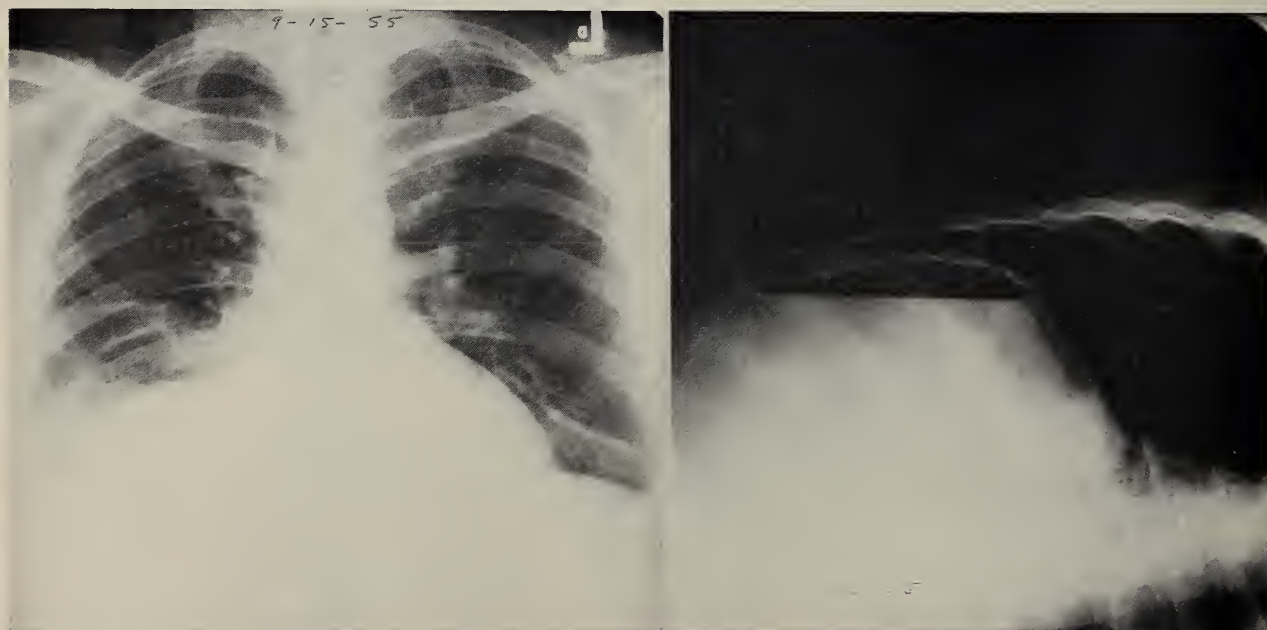


Figure 4.—Five weeks after the date of Figure 3 and two months after operation, the large cavity with an air-fluid level below the right hemidiaphragm is still evident, with persistent hypostasis at the right base and an elevated fixed right hemidiaphragm. The abscess was again drained.

was afebrile, regained 30 pounds and stated that he felt well. However, three or four weeks before the present admission to hospital, cough, malaise, anorexia and vague aching in the chest developed. Temporary improvement followed administration of vitamins and penicillin, but then all symptoms returned with fever and chills and the patient collapsed. On admission the temperature was 38.9°C (102°F). Leukocytes numbered 20,800 per cu mm, with 93 per cent polymorphonuclear cells. There were right basilar rales. Upper abdominal guarding and tenderness was noted, and the liver was palpable just below the costal margin. The patient had cough and dyspnea. The clinical impression was pneumonia.

X-ray films showed segmental atelectasis in the right lower lobe and an elevated right hemidiaphragm. Four days later, x-ray studies showed bilateral basilar infiltration with an air-fluid level below the right hemidiaphragm. The right subphrenic space was then drained of 150 ml of pus. Gradual improvement followed and there was no recurrence.

Differential Diagnosis

Immediately after operation in the upper abdomen, elevation and restricted motion of the diaphragm are normal findings. When these phenomena persist they may be secondary to either thoracic or abdominal complications. The commonly encountered lesions above the diaphragm that must be considered in the differential diagnosis of subphrenic abscess are infarct, atelectasis, basilar hypostasis, pneumonia and pneumonitis. Similar diaphragmatic findings may be associated with subphrenic inflammatory lesions either adjacent to the operative site, in the subphrenic, hepatic or subhepatic areas, or in the lesser sac. Therefore, the diaphragmatic findings present in subphrenic abscess are nonspecific and the diagnosis of abscess must be made by exclusion and by correlation with the clinical symptoms and the associated radiologic observations. When the ab-

scuss is indolent or in an early stage, the difficulties of diagnosis are compounded.

An air-fluid level below the diaphragm is usually indicative of abscess. Other confusing gas shadows may be due to postoperative air (which may persist for 10 days), to hydropneumoperitoneum or to interposition of the colon between the liver and the diaphragm. In one case of retroperitoneal abscess observed by the author there was an irregular gas shadow in the right abdomen, and another patient with a gas shadow had an abscess in the anterior abdominal wall. Extra-alimentary gas shadows were also seen in a patient with colonic-gallbladder fistula and in two patients with emphysematous cholecystitis. One patient with pain in the chest had subphrenic air due to a Rubin's test 24 hours previously which she had neglected to report to her family physician.

In one patient subphrenic abscess was diagnosed erroneously. The patient, a 58-year-old man, had had a sigmoid colectomy, and pelvic abscess developed five weeks later. At seven weeks he had right upper abdominal pain and fever and x-ray studies showed limited motion and elevation of the diaphragm, basilar pneumonitis and pleural reaction, but no air-fluid levels. He had been receiving heavy doses of five different antibiotics since the operation. At laparotomy after the clinical and roentgen diagnosis of subphrenic abscess, only edema and a pronounced inflammatory reaction under the diaphragm and over the dome of the liver were observed and there was no accumulation of pus. Six months later the patient was reported as "completely recovered."

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Cholelithiasis and Cholecystitis In Childhood

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■ *Six cases of cholecystitis and cholelithiasis confirmed by x-ray examination and surgical operation were observed in a ten-year period. Due to the wide variability in signs and symptoms in children, cholecystitis and cholelithiasis can be diagnosed only with a high degree of clinical suspicion and roentgenological examination. Gallbladder disease is uncommon in childhood but should be considered in children with vague abdominal pains or bouts of unexplained jaundice. If a normal appendix is found at laparotomy in the "acute abdomen," the surgeon would be wise to palpate other specific organs within the abdomen, including the liver and gallbladder.*

The treatment of choice is cholecystectomy. The prognosis for recovery is excellent if there is no complicating systemic disease.

SINCE GIBSON¹³ FIRST reported cholelithiasis and "an extraordinary large gallbladder and hydropic cystitis" in a 12-year-old boy in 1723, it has become apparent that cholelithiasis and cholecystitis are not rare diseases in childhood. Ulin and co-workers,³⁵ reviewing 475 case reports in the literature up to 1948, accepted 326 as substantially proved. Patients with disease elsewhere in the abdomen, such as peritonitis associated with perforated appendix or symptoms without operative or pathologic data, were eliminated. Glenn and Hill¹⁴ compiled 30 cases between 1948 and 1954, including seven of their own, and Lary and Howard¹⁷ added 12 cases reported between 1948 and 1959. Walker³⁶ reported nine additional cases from the Great Ormond Street Children's Hospital seen between 1940 and 1957, and Soderlund and Feterstrom³¹ reported 60 patients operated upon in the period to 1961 in Stockholm. Additional reports* have increased the total to over

560. The greater frequency of case reports during the past decade suggests that this cause of chronic abdominal pain in childhood is being recognized more frequently.

This report concerns six additional cases of cholecystitis with lithiasis in childhood which were proved by x-ray examination, subsequent operation and pathological studies. These illustrate most of the features of this problem and were seen between 1955 and 1965 in this hospital.

Report of Cases

CASE 1.—A 13-year-old Mexican girl had cholecystectomy with choledochoduodenostomy at age six weeks because of congenital choledochal cyst. Eight years later she began to have episodes of recurrent, sharp, localized epigastric pain unrelated to meals, with occasional nausea and vomiting. A 5×5 cm epigastric mass was palpated following an attack of pain in 1965. Physical examination was otherwise within normal limits. The patient was 140 cm tall and weighed 42 kg. Except for one serum glutamic oxalopyruvic transaminase determination of 96 units, results of all

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Submitted 28 September 1966 (revised 17 May 1967).

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*Reference Nos. 4, 8, 21, 27, 29, 32.

liver function tests including a liver biopsy were normal. The hemogram was normal. An intravenous cholangiogram indicated a patent biliary system. At operation, decided stricture at the site of the previous anastomosis was found. An operative cholangiogram revealed a dilated common duct with multiple 0.1 to 1.0 cm filling defects representing stones in both hepatic and common ducts (Figure 1). The liver appeared mildly cirrhotic both grossly and microscopically. Cholecolithotomy with reanastomosis of the common duct to the second portion of the duodenum was carried out. A year later the patient was asymptomatic and all liver function tests were within normal limits.

CASE 2.—A 14-year-old Caucasian boy had three attacks of moderately severe right upper quadrant abdominal pain and nausea following ingestion of fatty foods in 1964 and 1965. Between attacks, the patient had belching and flatulence after eating spicy foods. In February 1965 a double dose cholecystogram failed to visualize the gallbladder.

The mother and two sisters were obese. The mother had cholecystitis following the birth of the patient. There was no family history of blood dyscrasia.

Results on physical examination were within normal limits except for obesity: Weight 110 kg, height 170 cm. Results of all laboratory work, including liver function tests, were within normal limits. A chronically inflamed gallbladder containing multiple 0.4 cm mulberry cholesterol calculi was removed surgically in April 1965. The boy was asymptomatic thereafter.

CASE 3.—A six-year-old Caucasian boy was seen in the outpatient clinic in 1964 for dysuria and incontinence. In the course of a urological

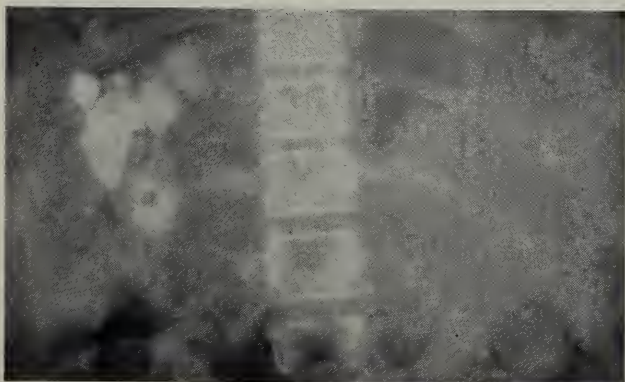


Figure 1.—Operative cholangiogram (Case 1) showing multiple calculi in dilated common and hepatic ducts.

investigation, an extrarenal calculus was noted in the right upper quadrant of the abdomen. An oral cholecystogram was done but the gallbladder was not visualized. A double dose of contrast medium was given, again without visualization. Intravenous cholecystography was necessary since absorption of the swallowed contrast medium was unsuccessful. The hepatic and common ducts were visualized and the contrast medium appeared in the duodenum but the cystic duct and the gallbladder retained no dye. Results of all blood chemical studies, including liver function tests, were normal except for eosinophilia. Cysts of *giardia lamblis* were noted in the stool. Physical examination was within normal limits. The patient's height was 108 cm (50th percentile) and the weight 24.5 kg (80th percentile).

Cholecystectomy was done and at operation a thick-walled contracted gallbladder with 1.4×1.5 cm calculus in the cystic duct was found. The post-operative course was uneventful.

Plain films of the abdomen on all members of the immediate family were obtained, although none had had gallbladder disease. No calculi were identified.

CASE 4.—A three-year-old Mexican boy was admitted to hospital in April 1960 because of ingestion of hydrocarbon. An x-ray film of the chest included the upper abdomen, and three calculi were seen in the right upper quadrant (Figure 2). A subsequent oral cholecystogram identified these as gallstones. Retrospectively, the child had complained of short attacks of general abdominal pain four times in the previous year. There had been no nausea, vomiting or food intolerance. The fam-



Figure 2.—Radiograph of the abdomen (Case 4) shows three calculi in the right upper quadrant.

ily history was negative for gallbladder disease or hemolytic anemia. No abnormalities were noted on physical examination. Results of laboratory work, including liver function tests, were within normal limits.

Two months later, elective cholecystectomy was performed. The gallbladder contained three black calculi, the largest 1 cm in diameter. Microscopically the gallbladder walls were chronically inflamed. The child was asymptomatic after operation.

CASE 5.—An 11-year-old Mexican girl began to have pains in the right upper quadrant of the abdomen 14 months before admission to hospital in February 1959. The pains were precipitated by ingestion of fatty foods, were accompanied by nausea and vomiting, radiated to the left upper quadrant and right scapular area and lasted for periods of a few minutes to several days. Gallstones were noted when an intravenous pyelogram was taken following a urinary tract infection in January 1959 (Figure 3). There was no history of anemia or jaundice. The mother had had cholelithiasis at the age of 30. Results of physical examination were within normal limits. The patient weighed 35 kg and was 143 cm tall. On examination of the blood, eosinophilia was noted. The response to a skin test for trichinella was 4 plus, and cysts and trophozoites of *Enteromonas hominis* were observed in the stool. Results of all other laboratory tests were within normal limits.

The gallbladder was removed and two 0.5 cm calculi were noted within it. Microscopically, the gallbladder walls were normal. The patient was asymptomatic after operation.

CASE 6.—A Mexican boy two and a half years old was admitted in August 1955 for elective circumcision because of redundant prepuce. A firm non-tender moveable mass, possibly attached to the liver, was palpated in the right upper abdominal quadrant. A plain film of the abdomen revealed three distinct calcifications in this area, and a cholecystogram showed they were in the gallbladder. There was no history of jaundice, abdominal distress or anemia. The patient's mother complained of much right upper quadrant abdominal pain, but a cholecystogram seven years previously had shown no abnormality. A sibling also had much right upper quadrant pain but gallbladder studies did not show pathologic change.

During the following six weeks the patient had two episodes of icterus lasting one day each. He also had vomiting associated with ingestion of pork. He was readmitted in September 1955 for cholecystectomy. At that time he weighed 15 kg and was 93 cm tall. Results of physical examination were within normal limits. The only abnormality noted in laboratory test was serum cholesterol of 344 mg per 100 ml.

Cholecystectomy and liver biopsy were carried out in October 1955. The gallbladder contained several small stones. The liver was not enlarged

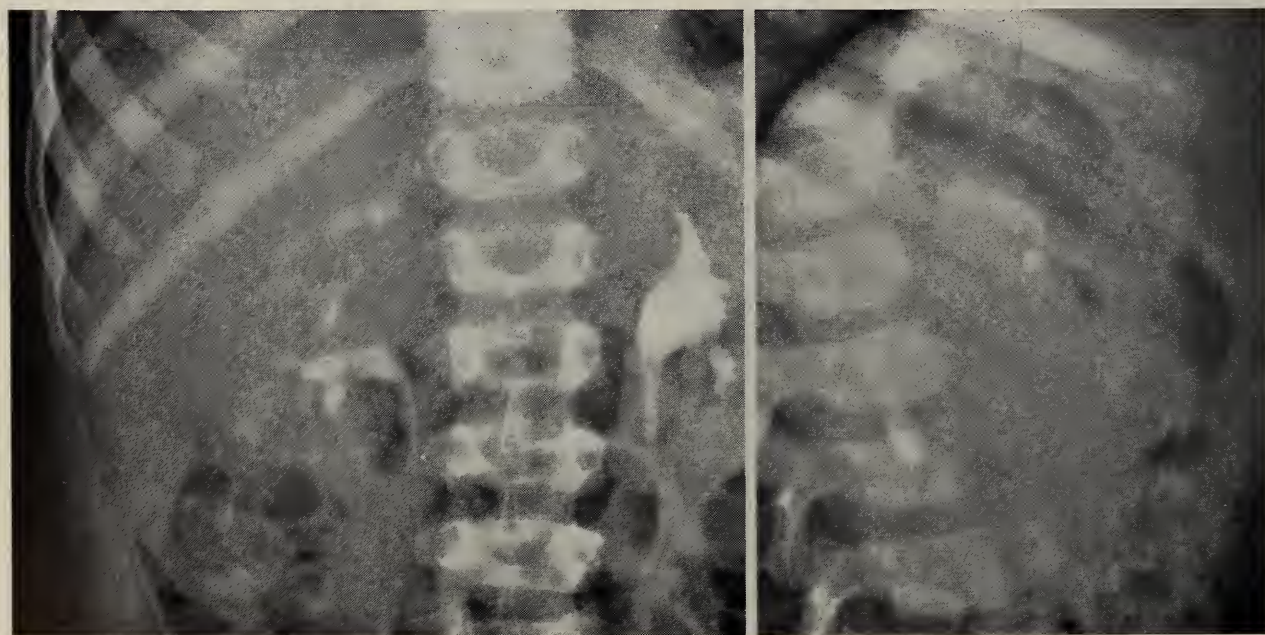


Figure 3.—Intravenous pyelogram (Case 5) shows calculi over the kidney on the lateral view in the region of the gallbladder.

but was exceedingly firm and fibrotic. On microscopic examination, mild acute cholecystitis and biliary cirrhosis were noted. The patient was entirely asymptomatic from then on. Liver function tests repeated in August 1963 showed serum transaminase of 35 units, total serum bilirubin 0.6 mg, direct bilirubin 0.3 mg per 100 ml, and thymol turbidity of 3 units.

Discussion

Incidence

The incidence of gallstones seems to vary throughout the world. They are rarer in India (5.4 per cent)³ than in the United States or Europe (10 per cent).^{10,18} The lowest incidence is reported in China (2.2 per cent) and in Russia (2.2 per cent).²⁰

Stones in children are uncommon. Autopsy records show an incidence of 0.28 per cent.³⁸ Glenn and coworkers¹⁴ noted only two cases of primary gallbladder disease with stones in 20 years at the Cornell Medical Center, but excluded all cases secondary to hemolytic anemia. Seiler²⁷ found seven cases, all with stones, at Strong Memorial Hospital in Rochester in a 10-year period. Walker³⁶ noted nine cases in 17 years at Great Ormond Street Hospital. We have found six cases in our records over the past 10 years.

Etiology

The cause of cholelithiasis in childhood, with the exception of hemolytic disease, remains obscure. Statements of investigators conflict on many points having to do with possible etiological factors.

Reviews of large series of cases have failed in a great majority to elicit a strong family history of disease, although the pedigree has not been followed far in most cases. However, several small series^{27,11,32} indicates an incidence of gallbladder disease in over 50 per cent of the patients' families. Gallstones have been found in identical twins.³⁴ The members of the immediate family of the patient in Case 1 herein reported were examined roentgenographically for opaque silent stones, but none were found. Two of the six patients in the present cases had a family background of gallbladder disease.

Gallbladder disease affects adult females four times more often than adult males. In childhood the incidence of gallbladder problems is also higher in females than males in ratios up to 10:1. Our series included four boys and two girls.

Two investigators have commented on obesity in this disease in childhood.^{12,27} Two of the six patients reported herein were over the eightieth percentile in weight. No direct and constant relationship between the cholesterol content of bile and that of serum has yet been demonstrated.

Cholelithiasis has been noted frequently in malformations, especially stenosis of the biliary ducts, which contribute to bile stasis.^{12,31,36} We found a surgically acquired malformation in one child.

Contagious and systemic diseases such as typhoid fever, scarlet fever, gastroenteritis and septicemia have been associated with cholecystitis. Gallbladders removed from children with cholecystitis invariably show an infiltration of the walls by polymorphonuclear leukocytes and bacteria.^{10,35} However, the bile ducts are usually free of infection and the bile sterile at the time of operation.¹⁰ Lithiasis cannot be produced experimentally in animals either by stasis or infection even in the presence of foreign bodies.¹¹

The role of intestinal parasites is interesting and two of the patients reported upon herein had infections and secondary eosinophilia. *Ascaris lumbricoides* has been reported as a source of gallbladder infection.^{1,6} *Giardia lamblia* has been found in the duodenum of children with gallbladder disease^{26,28,39,40} but direct evidence is lacking that these parasites were primarily pathogenic.

Hemolytic anemia, acute or chronic, is reported as a common cause of cholelithiasis in childhood.^{15,27,36} In Negro children with sickle cell anemia, the incidence of cholelithiasis is 9.5 per cent,¹⁹ but often the stones are asymptomatic and rarely require surgical intervention. Most stones associated with sickling occur in older children and are not found in the first decade, according to Weems.³⁷

Stone Formation

Gross' statement¹⁵ that cholelithiasis is more common than acute cholecystitis is apparently correct when large series of cases are considered. Ulin's³⁵ review of reported cases indicated a 69 per cent incidence of stones in the gallbladder. Potter²² found only a 51 per cent incidence. Other reports of smaller series of cases show stones in 67 of 75 cases.^{12,27,31,36}

Choledocholithiasis is considerably rarer than stones within the gallbladder itself. Ulin³⁵ found the relative incidence in a series of 350 cases was 6 per cent and 17 per cent. Although Potter²² found that calculi occur with equal frequency in

the cystic and common ducts (4.7 per cent and 4.3 per cent respectively), recent reports of cystic duct stones are most unusual.^{12,27,31,36} In our series we noted one large asymptomatic stone in the cystic duct of one patient, and stones in the common duct of another child who had previously had cholecystectomy.

Signs and Symptoms

The classic adult symptoms of gallbladder disease are usually lacking in childhood, as in the present series. Gallbladder disease, although uncommon, must be considered in the differential diagnosis of vague abdominal pain and jaundice in children. Intermittent colicky abdominal pain, of varying intensity, occasionally so severe as to require narcotics, occurs in at least 95 per cent of all cases. The pain is localized below the right costal margin in two-thirds of the patients and is periumbilical or not localized in the remainder. Children under six years of age especially have difficulty localizing the pain. Radiation to the back and right shoulder is generally uncommon, although it was reported in half the cases of Soderlund.³¹

When a stone becomes lodged in the cystic duct, pain is usually severe. The origin of the pain may be associated with such factors as spasm or contraction of the gallbladder, distention of the duct, or inflammation associated with the stone itself. The pain is usually paroxysmal, with tenderness in the right upper quadrant of the abdomen. Occasionally the stone can be silent and asymptomatic as in Case 3 herein.

The pains may appear in infancy as early as three to six months of age.^{14,30,36} However, the average age of onset is eight to ten years.³⁵ The difficulty in making the diagnosis is apparent from the average interval between the onset of symptoms and the correct diagnosis—four and a half years. The pain is often mistaken for that of acute appendicitis. One patient in six undergoes appendectomy before the cause of the pain is correctly determined.

Nausea and vomiting accompany the pain in about 75 per cent of cases. Many of the children become listless and anorexic and complain of fatigue and aching during attacks. In contrast to the frequency of these symptoms in adults, food idiosyncrasy, feeling of fullness and belching are uncommon.

The low incidence (6 per cent) of common duct stones but the high frequency of jaundice (up to

66 per cent) is of interest.^{22,35} Frequently the cause has been attributed to hepatitis or has been undetermined. Investigations have shown only a moderate rise in bilirubin.

Jaundice occurs in only half of the cases of common duct stones. It is ascribed to obstruction of the bile passages by inflammation and spasm, leading to interference with the flow of bile similar to that of obstruction of ducts by stones in adults. In some cases the inflammation may be due to a process adjacent to the ducts, such as lymphadenitis or to inflamed diverticuli of the ducts themselves.³⁵ Silent stones in the ducts and gallbladder also occur, inflammation being absent in up to a third of the cases at operation. Babbitt⁴ reported two cases of stones in ducts with no symptoms for months, and one of the patients in the present series never had symptoms despite the presence of a large obstructing stone in the cystic duct. It is possible that in many cases of acholuric hepatitis or congenital hepatitis or congenital hemolytic anemia there are stones which are clinically undetected.

The only other signs noted have been tenderness in the right upper quadrant of the abdomen and occasionally slight enlargement of the gallbladder or the liver. Younger patients may have signs of "acute abdomen" due to cholecystitis, and the onset may be fulminating. Laparotomy may be required before the diagnosis is made.

The laboratory is of no assistance. Increases in serum bilirubin up to 6 mg per 100 ml of serum have been noted. Blood cell count and sedimentation rates are usually normal. Rarely, the stools are clay-colored. Blood electrolytes and cholesterol are within normal limits. However, the presence of lithiasis as observed by x-ray examination would indicate a search for hemolytic anemia.

Diagnosis

The diagnosis depends on demonstration of the calculi on the cholecystogram. In our series several of the patients were fortuitously discovered to have gallstones on films ordered for intravenous pyelography or films of the abdomen taken for some unrelated reason. An oral cholecystogram is the examination to be first employed; if the gallbladder does not fill, a double dose is mandatory. On rare occasions an intravenous cholangiogram is indicated.

Treatment

Cholecystitis and cholelithiasis in childhood are dealt with surgically much as the disease is in

adults. Cholecystectomy is the treatment of choice in cholecystitis unaccompanied by stones. The procedure is invariably curative, although up to 20 per cent of patients who are operated upon may complain of mild pains or food intolerance for more than a year afterward.³¹ The six patients reported upon herein have been observed for periods up to ten years with no recurrence of symptoms although in two children liver biopsy revealed mild biliary cirrhosis.

Immediate treatment of acute cholecystitis that is due to a systemic process such as typhoid or septicemia should be conservative. Antibiotics, sedation, parenteral fluids and rest may tide the child over the acute episode. If the patient does not respond to these measures but remains febrile and acutely ill, and the leukocyte count rises, exploration may be necessary to arrest the spread of infection.¹⁵

Cholecystectomy is also usually necessary in cholelithiasis if the calculi lie entirely within the gallbladder. Although duct stones are unusual, the common duct should be investigated by operative cholangiography, especially if jaundice has been present.

If the patient has congenital spherocytic anemia with cholelithiasis, Gross¹⁵ prefers to correct the hemolytic process by splenectomy first and then remove the calculi at a subsequent operation. If a high grade of common duct obstruction is present, the duct is explored first and splenectomy deferred. The combination of cholecystectomy and splenectomy at a single operation carries high risk of severe or fatal shock according to Gross.¹⁵

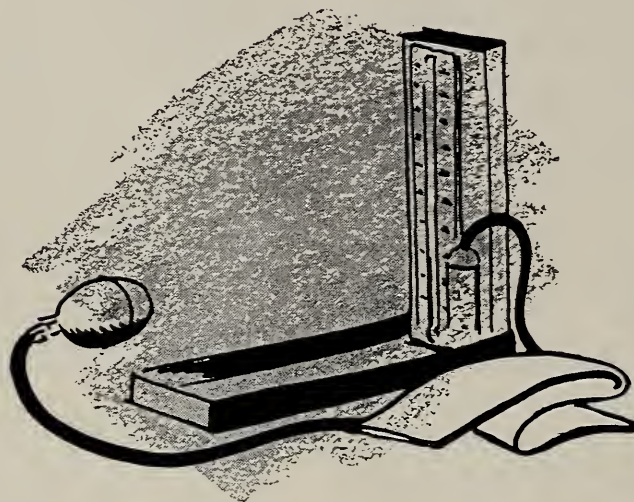
The crisis to sickle cell and other hemolytic anemias must be differentiated from biliary obstruction and inflammation, since surgical mortality also rises during these periods. Jaundice of hepatocellular origin is much more common than gallbladder diseases, and surgical operation in this condition is contraindicated. Gross¹⁵ suggested that a high icteric index with acholic stools, abdominal pain and vomiting is indicative of extrahepatic biliary obstruction. If cholecystitis cannot be differentiated from appendicitis, and the child's condition warrants operation, laparotomy is advisable.

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Pressor Agents

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THE ROLE OF PRESSOR AGENTS in clinical practice is controversial. However, the use of these drugs is so widespread that a discussion of their pharmacologic properties and an assessment of their actual usefulness is justified. Thus this review will first deal briefly with classifications and mechanisms of action of these drugs, and then describe individual agents, grouping them by pharmacologic actions. This description, coupled to a knowledge of the patient's hypotensive state, should enable us to evolve a more effective therapeutic regimen. Unfortunately, the wide gaps in knowledge in both areas hinder the attainment of this goal.

In describing the actions of pressors, the effects on the circulation as a whole will be stressed. It must be borne in mind that any change in the systemic circulation does not necessarily indicate a similar change in flow to various organs. A discussion of these latter events is beyond the scope of this review.

Most of the studies to be cited have been performed in normal humans or in animals. These results cannot be reliably extrapolated to drug actions in man during shock, but unfortunately there are few well-controlled studies on this subject.

Definition

A pressor drug is an agent which elevates blood pressure above its existing level. Most of these agents belong to a class of drugs called sympathomimetic amines, which are derivatives of phenylethylamine. There are also two polypeptides in current use—angiotension and PLV-2 (2-phenylalanine, 8-lysine vasopressin).

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Supported by Program Project No. GM-12527, Army Contract No. DA-49-193-MD-2135 and NIH Development Award No. 1-K3-GM-31-757.

Submitted 3 November 1966.

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Pressor agents are used presumably because the arterial blood pressure is "too low," although often the blood pressure is a poor indicator of the circulatory status of the patient, for there may be excellent tissue perfusion even though arterial pressure is low. This occurs during peripheral ganglionic blockade. On the other hand, pressure may be elevated, yet at the expense of such intense vasoconstriction and poor tissue perfusion that death may be inevitable in a few hours if the situation is not corrected. Nevertheless, since blood pressure is an easily obtained measurement, it will remain as a guideline to therapy. Too often, however, we want to correct the blood pressure mainly because it is low; it is ourselves, not the patient whom we are treating.

Causes of Hypotension

Since a knowledge of the mechanism of decreased blood pressure in a given patient can aid in the selection of proper therapy, it may be useful to list some of the causes of low blood pressure:

"Shock"—including conditions caused by hemorrhage, sepsis, endotoxin, trauma, burns or any combination of these factors.

Myocardial failure, especially that accompanying acute myocardial infarction.

Arrhythmia, especially extreme tachycardia.

Reflexes, particular vagal reflexes—for example, the carotid sinus reflex.

Drugs, which induce either a direct myocardial depressant action or peripheral vasodilation, or both. They include anesthetic agents, ganglionic blocking agents and various other types of antihypertensive agents and potent tranquilizers.

Sympathetic blockade, which may be chemical (spinal or epidural anesthesia) or surgical.

Mechanisms of Vasopressor Action

An easy way to remember the basic regulation of blood pressure is the formula: $\overline{AP} = CO \times TPR$,* where \overline{AP} = mean arterial pressure, CO = cardiac output, and TPR = total peripheral resistance. Thus, mean arterial pressure may be increased by raising cardiac output or total peripheral resistance, or both. Cardiac output may be increased by an increase in myocardial contractility, in heart rate or in the amount of blood presented to the heart, the latter usually an increase in venous return to the right side of the heart. Venous return is commonly increased by decreasing the capacity of the veins—that is, by venoconstriction. Total peripheral resistance is elevated mainly by arteriolar constriction. Very little increase in resistance is achieved by constriction of the large arteries.

Vasoconstriction can affect cardiac output in different ways: (1) Arteriolar constriction raises total peripheral resistance and decreases cardiac output; (2) pre-capillary constriction decreases capillary hydrostatic pressure, shifting fluid from tissue to capillaries and resulting in an ultimate increase in cardiac output; (3) venous constriction increases venous return and increases cardiac output; or (4) post-capillary constriction impedes outflow from the capillaries, and causes increased capillary hydrostatic pressure with a loss of fluid from capillaries to tissues and an ultimate decrease in cardiac output.¹⁰⁷ The relative strength of action of a drug upon these vascular beds is important in selecting a drug. Table 1 shows the average percentage contribution of increments in venous resistance to increments in total resistance ($\Delta VR / \Delta TR \times 100$).¹⁷⁵ Note for example that norepinephrine and methoxamine, both considered to be potent "vasoconstrictors," differ decidedly in the effect they have on the veins. This table will be referred to throughout the review.

Classification of Pressor Agents

The action of vasopressors may be understood by referring to three classifications: (1) The target organs stimulated (heart vs. blood vessel or central vs. peripheral), (2) the type of action on the receptor sites (direct vs. indirect), and (3) the type of adrenergic receptor site stimulated (alpha vs. beta). "Central" and "indirect" actions of vasopressors do not refer to any action mediated by the central nervous system.

*This, of course, is analogous to Ohm's Law in electricity: $E = IR$, where E is the voltage (pressure), I is the current (flow), and R is the resistance.

Heart vs. blood vessels. The cardiac actions of pressors are those of increased strength of contraction (positive inotropy) and increased heart rate (positive chronotropy); the blood vessel action that of vasoconstriction. This is the best clinical classification for selecting a pressor. There are no pressor drugs which are exclusively central in action. Methoxamine and phenylephrine are prototypes of pure peripheral vasoconstrictors.⁷ Most drugs fall in a spectrum ranging from marked central and weak peripheral to marked peripheral and weak central action. Although there is no substantial agreement on the relative position of most of the individual pressor agents in this spectrum, it is possible to group agents together by their relative central and peripheral actions. This will be the classification used in the present review.

Direct vs. Indirect Action. Direct action implies stimulation of the receptor sites by the drug itself, while indirect action implies stimulation by a secondarily released transmitter substance, such as norepinephrine or isoproterenol. Examples of the direct group of drugs are epinephrine,⁷⁰ norepinephrine,⁷⁰ methoxamine,⁷⁰ phenylephrine,⁷⁰ angiotensin,¹³¹ and PLV-2.⁷⁰ The action of all other drugs discussed in this review has been attributed at least in part to the indirect mechanism: Mephentermine,⁶ amphetamine,³⁰ methamphetamine,³⁰ metaraminol,⁶ and ephedrine.³⁰

The theory of indirect action originated with Burn and Rand,³⁰ who observed that animals pretreated with reserpine, guanethidine or bretylium did not respond to ephedrine, amphetamine, methamphetamine or tyramine. This theory, along with clinical observation, led to the belief that patients under therapy with reserpine or guanethidine would experience severe hypotensive episodes during anesthesia—hypotension which was refractory to many of the pressors.^{32,119,153,174} This theory was also the basis for the ephedrine response test, which attempted to predict which of the patients on antihypertensive therapy were liable to develop refractory hypotension during anesthesia.³⁶ To perform this test, a standard amount of ephedrine was administered intravenously. A normal pressor response foretold a safe anesthetic course. No response, or a hypotensive response, indicated the discontinuation of anti-hypertensive therapy for two weeks before elective surgical operation was permissible.

Recent investigations have shown that patients on reserpine can undergo anesthesia and surgical

operation without added hazard^{123,166} and that animals treated with reserpine show no significantly different response to anesthesia than untreated animals.^{9,10,137} Depression of the pressor response to the indirectly acting vasopressors does not occur in the presence of fully effective doses of reserpine, guanethidine or bretylium.^{95,98} Ephedrine has definitely been shown to have a direct effect of its own.^{81,170} Thus it is usually not necessary to withdraw reserpine or guanethidine before operation. Furthermore, these patients should usually respond well to all types of pressors. The conflicting results obtained with the ephedrine response test (by Crandell³⁶ and Hamelberg⁷⁵) are better understood in light of the above information.

Alpha and beta adrenergic receptors. Another review would be required to do justice to this concept. It will be mentioned briefly here, since it is useful in the understanding of pressor action. In 1948, Ahlquist¹ explained differences in action of norepinephrine and epinephrine on various sympathetic effector organs by postulating two different adrenergic receptor sites. The "alpha" receptors are responsible for vasoconstriction, intestinal relaxation and pilomotor contraction, while the "beta" receptors are responsible for vasodilation in the skeletal muscle, increased heart rate, increased myocardial strength, and bronchial and uterine relaxation. The prototype of the alpha-stimulating drug is methoxamine, which has a pure vasoconstrictor effect.¹²¹ The prototype of the beta-stimulating drug is isoproterenol, which produces tachycardia, bronchodilation, increased myocardial contractility and increased cardiac output, but causes decreased blood pressure because of pronounced overall peripheral vasodilation.¹²¹ Most sympathomimetic amines have a mixture of alpha and beta effects. The relative strength of each component is dose-dependent. Thus epinephrine at very small doses has strong beta and relatively weak alpha effects. As the dose increases, alpha effects begin to predominate.⁷⁰

Discussion of Specific Drugs

With this brief background, specific drugs will be discussed. These drugs will be grouped by their similarity in effect, although there is little agreement on the precise action of any pressor agent. More recent investigations will be emphasized; hence, some agents will be dealt with more extensively than others.

Epinephrine. Epinephrine stands in a group by itself. It raises systolic blood pressure by increas-

ing cardiac output, myocardial contractility and heart rate and by producing some venoconstriction.² In smaller doses, it may actually lower total peripheral resistance⁷, but the other actions usually compensate for this decrease. Although a reliable and powerful agent, it is not used routinely because of its metabolic and severe arrhythmic effects. However, there is a resurgence of popularity for its use in the critical situation—that is, in cardiac arrest. Pearson and Redding^{133,135} showed that after hypoxic cardiac arrest in dogs, the survival rate is higher in those animals treated with epinephrine. This was true even when ventricular fibrillation was present. It appears that the intracardiac injection of epinephrine is indicated even before an electrocardiographic differentiation between asystole and fibrillation is made, provided the myocardium is well-oxygenated by proper pulmonary ventilation and cardiac massage.

Norepinephrine and Metaraminol. These agents have similar effects, stimulating both alpha and beta receptors, with a predominance of alpha stimulation.^{24,121} Norepinephrine acts directly while metaraminol may act indirectly by the release of norepinephrine.²² The latter hypothesis is corroborated by the fact that after metaraminol is administered, the radioactivity issuing from a heart labelled with tritiated norepinephrine appears almost entirely as bases (norepinephrine and normetanephrine), suggesting that metaraminol, like guanethidine, releases norepinephrine from the granules.²⁴ Metaraminol is an exceedingly potent depleter of norepinephrine in the peripheral vessels^{16,96} and the atria.^{16,22} These observations help explain common clinical observations—a progressive diminution in response to the repeated or continuous administration of metaraminol (tachyphylaxis),³⁸ and a loss of the positive chronotropic response to hypotension.²¹ By depleting the norepinephrine stores in sympathetic nerve endings in the heart and blood vessels, prolonged infusions of metaraminol may result in a diminution of sensitivity to subsequently administered metaraminol. Discontinuing metaraminol and infusing norepinephrine for a period restores the response to metaraminol.²² This is presumably due to repletion of norepinephrine stores at the sympathetic nerve endings.

Not only does metaraminol deplete norepinephrine, but it may actually replace it at the storage sites.¹⁵² This property is similar to that postulated for the metabolic products of alpha-

methyldopa, an antihypertensive agent.^{75,93} These compounds are now available for release by stimulation of sympathetic nerves or by drugs, such as tyramine. Thus they may act as "false transmitters" in place of norepinephrine.^{38,152} Since they are considerably less potent than norepinephrine, the effect produced by any release is proportionately less. This suggests that metaraminol might be useful as an antihypertensive agent. Indeed, Crout and coworkers³⁹ have successfully used metaraminol orally to lower blood pressure in hypertensive patients. Thus, paradoxically, one of the most potent vasopressors can also be used to lower blood pressure.

Norepinephrine has marked positive inotropic and chronotropic (beta-adrenergic) actions, the inotropic effect being equal to that of epinephrine and of isoproterenol in equivalent doses.^{27,44} But it produces such intense vasoconstriction, with a consequent increase in total peripheral resistance and blood pressure, that reflex vagal action produces bradycardia and occasionally decreased cardiac output.^{2,7} There are some advantages to the use of norepinephrine as a pressor agent. It practically never fails to elicit a pressor response—at least initially. This response occurs even when other agents are ineffective.⁷⁰ Since the pressor effect of norepinephrine disappears within a few minutes after discontinuing the drug, titration of blood pressure may be achieved by infusion.⁷⁰ The dangers of overdosage and marked hypertension are thus lessened. According to Sayen and coworkers¹⁴⁶ norepinephrine may increase the availability of oxygen to the myocardium during shock as determined by oxygen tension measurements using oxygen electrodes. Ribeilima and associates¹³⁸ also believe that there is increased availability of oxygen to the myocardium in normal human subjects during infusion of norepinephrine. Meier and coworkers¹¹⁸ recently showed that norepinephrine increases coronary blood flow and myocardial oxygen consumption in equal proportions. However, not all investigators agree with the above results, as will be noted later.

Norepinephrine has many more disadvantages than advantages. Some of these are peculiar to the drug itself; others are related to a recent reexamination of the role of pressor agents in general. If norepinephrine leaks from a vein into the surrounding tissues, severe ischemia and sloughing may result.²⁸ This can be prevented by adding 5 to 10 mg of phentolamine per 4 mg of norepinephrine in the infusion bottle.¹⁷⁶ Phentolamine will

block the more severe alpha action (constriction) caused by high local concentration of norepinephrine. Arrhythmia, occasionally serious, can result from use of the drug, particularly during anesthesia with such agents as cyclopropane.⁷ There is decreased blood flow to many tissues, resulting in circulatory stasis and acidosis, capillary fluid loss and, eventually, in hepatic, renal and bowel necrosis.¹⁰⁴

Norepinephrine can produce a state of shock indistinguishable from late hemorrhagic, traumatic or endotoxic shock.¹⁰⁴ In dogs, heart failure will result from an infusion of 2 to 4 micrograms per kilogram of body weight per minute, given over a period of 30 to 60 minutes.^{73,122} This failure is accompanied by cardiac lesions characterized by subendocardial and epicardial hemorrhages and focal myofibrillar degeneration and necrosis.^{73,147,159,160} This response is time-dose dependent. Thus, an infusion rate of one microgram per kilogram per minute will induce failure in several hours.

The cause of the myocardial lesions is still obscure. It has been speculated that myocardial hypoxia is a major factor.^{122,139} After an infusion of more than an hour, norepinephrine continues to augment the rate of myocardial contraction, and hence the oxygen consumption, without continuing to elevate arterial pressure.¹²² Since norepinephrine does not dilate coronary arteries directly,¹⁷² any increase in coronary flow necessary to supply the oxygen must be achieved by an increase in arterial pressure. However, it has become evident that the similar myocardial lesions produced by isoproterenol can be modified by complex interactions with other catecholamines,⁵⁶ with mineralocorticoids³¹ and with electrolytes.¹⁴⁰ It is interesting that these lesions resemble quite closely those of human coronary artery disease.⁵⁶

Pulmonary edema is occasionally seen, apparently brought about by a different mechanism than that causing shock. Norepinephrine can produce a decided shift of blood volume from the systemic to the pulmonary circulation.¹¹⁵

Norepinephrine also presents the problem of tachyphylaxis, but on a different basis from metaraminol. This does not occur so frequently as with ephedrine or metaraminol, but it is more serious, since norepinephrine is often used after other agents have failed. Many theories have been proposed to explain this disturbing phenomenon: (1) Secondary dilation of the veins.¹¹⁵ (2) Ganglionic block induced by norepinephrine or one of its

metabolites.^{45,109,114} (3) Acidosis produced by circulatory stasis, causing a decreased response to norepinephrine.⁴² (4) Formation of vasodilator substances consequent to prolonged infusion.^{19,47,99} (5) The myocardial lesions mentioned above. (6) Storage of infused norepinephrine in arteries with consequent unresponsiveness to norepinephrine.²⁹ (7) Decrease in plasma volume. The last is the most attractive hypothesis to date.

Studies by Mazurkiewicz and Murnaghan,¹¹⁵ using hexamethonium as well as sympathomimetic amines with better ganglionic blocking properties than norepinephrine, leave considerable doubt as to the validity of hypotheses Nos. 2 and 4 in the foregoing paragraph. Myocardial lesions develop a long time after the onset of tachyphylaxis and, therefore, cannot be completely responsible for the tachyphylaxis. Restoration of any decrease in pH to normal levels does not restore reactivity to norepinephrine,¹⁴² thus making acidosis unlikely as a cause of tachyphylaxis. On the other hand, infusion of norepinephrine does lead to a decrease in plasma volume with hemoconcentration in animals^{60,149} and in normal subjects after hemorrhage.¹⁰⁷ This decreased plasma volume can be prevented with alpha-blocking agents, such as phenoxybenzamine, and treated with plasma infusion.¹⁴² These same measures can prevent or be used in treating tachyphylaxis. The phenomenon is similar to the blood pressure drop observed after removal of a pheochromocytoma.¹⁶⁵ This drop is preceded by excess serum norepinephrine levels and by a decrease in red cell volume,⁶⁹ and can be prevented with phentolamine pretreatment¹⁶⁵ or excess blood volume replacement.¹¹³ According to Lister and coworkers¹⁰⁷ the mechanism of decreased plasma volume with norepinephrine infusion is post-capillary (venular) constriction. This raises capillary pressure with a resultant shift of fluid out of the circulation. Angiotensin, which produces a selective pre-capillary constriction, induces far less tachyphylaxis.

Bendixen and coworkers¹¹ have shown in anesthetized dogs that the differential action of norepinephrine is dose-dependent; that is, with very small doses the cardiac effects far outweigh the constrictor effects. But as the dose is increased, constrictor effects begin to predominate. They postulated that the use of large doses and a long infusion is a poor substitute for the more judicious amounts usually employed by the organism.

All of these statements are distressing to those of us who may think in a teleologic manner. Nor-

epinephrine is a naturally occurring substance. How can one justify the presence of a substance which seems to be so harmful under so many circumstances? Nickerson¹²⁵ believes that in nature, prolonged shock rarely occurs. If an animal suffers severe shock, it is usually unable to escape from the causative factor. Only man has been able to carry severe shock past its acute stage and thus witness the deleterious effects due to the therapeutic abuse of a life-saving agent.

Ephedrine and Hydroxyamphetamine. These agents manifest both cardiac and peripheral constrictor effects, with the cardiac effects predominating.^{5,173} Thus tachycardia, increased cardiac output and increased stroke volume are common.

Ephedrine is theoretically an ideal agent to reverse hypotension from the sympathetic block due to spinal or epidural analgesia. Block of this type causes venous pooling, decreased peripheral resistance, decreased cardiac output, occasionally decreased myocardial contractility and decreased heart rate.⁷² Ephedrine acts as a physiologic antagonist to all of these depressant actions. The incidence of arrhythmia from ephedrine administered during general anesthesia is not so great as with many other centrally stimulating amines.^{124,130} However, it is not a completely reliable drug; that is, it does not always produce a satisfactory pressor response.⁷ Rapid tachyphylaxis is often encountered with repeated injections.^{7,70}

Methoxamine and Phenylephrine. These two drugs are ostensibly very similar. They both act peripherally with no direct effects on the myocardium; that is, there is all alpha and no beta stimulating effect.^{6,78,102,121} Both agents act directly on the vessels with no hint of release of catecholamines.^{6,148,175} However, methoxamine has some properties of its own which may be very important. No investigations directly comparing the two drugs have been reported.

Because of its pure vasoconstricting action, methoxamine may actually be disadvantageous in many situations. Duke and coworkers⁴⁶ observed that an increase in blood pressure was achieved by an increase in cardiac work, peripheral resistance, venous pressure and central blood volume. But all of this effort only maintained the status quo in cardiac output. Presumably, then, there was a pronounced decrease in flow to many tissues. The price for increased ventricular work is an increase in oxygen consumption.¹⁴³ Although it has been pointed out that methoxamine increases coronary

blood flow,¹¹² a considerable increase in flow is necessary merely to keep up with additional oxygen demands. Li and his associates¹⁰² noted no significant change in cardiac work, but a decrease in cardiac output. Therefore, the same relationship between total flow and work still exists: An increase in cardiac work over the total flow obtained for that work.

There are indications that any pressor effect achieved by methoxamine is costly in other ways. Harrison and coworkers⁷⁸ measured right and left ventricular dimensions in conscious human subjects. Intravenous infusion of methoxamine produced a consistent increase in the volume of the left ventricle during all phases of the cycle. In other words, there was an acute cardiac dilation. These changes occurred even with a steady heart rate. It was felt that when resistance to ventricular outflow was increased by methoxamine, the left ventricle, in order to develop a higher systolic pressure, was obliged to increase its size. This increase in dimension, especially in systolic volume, could also explain the increases in stroke index, and occasionally in cardiac index, noted with the drug. This is obviously not a very efficient way to increase cardiac output.

Table 1 shows that methoxamine produces considerably less venous constriction than it does arterial constriction. There is evidence that methoxamine may thereby actually produce pooling of blood by peripheral trapping.¹⁰⁴ If so, this is a new action for pressor amines. All these considerations make methoxamine theoretically a poor drug to use in reversing the hypotension of spinal anesthesia. Li and coworkers¹⁰² expressed belief that methoxamine, because of its effects on hemodynamic factors, was satisfactory in treating patients who had a drop in cardiac index after spinal anesthesia. However, only three out of their seven patients showed an improvement in cardiac index, three others actually showing a further decrease

in cardiac index. Moreover, some of these patients had virtually a total sympathetic block, with a sensory level up to the third thoracic segment. Braunwald and his coworkers^{23,62,141} showed that in human subjects, in whom sympathetic influence on the heart has been removed, the responses of the heart to increased peripheral resistance or venous return essentially obeys Starling's law. Therefore, it is probable that an even greater cardiac dilation than observed by Harrison and coworkers⁷⁸ may occur with the use of methoxamine in high spinal anesthesia.

Another disconcerting finding was reported by Ellis.⁵² He administered methoxamine plus sodium EDTA (ethylenediamine tetracetic acid), an agent which binds ionized calcium. Arterial pressure, instead of rising, fell to very low levels. Other signs of cardiac failure were present. Ellis attributed this phenomenon to excitation-contraction uncoupling, particularly since mechanical alternans without electrical alternans was noted. Excitation-contraction coupling involves the proper conversion of electrical to mechanical energy, and any diminution of this conversion reduces the strength of the heart. It is also possible that myocardial depression from calcium-chelation plus intense vasoconstriction could have led to cardiac failure, though the absence of the phenomenon, when the animals were pretreated with reserpine, is against this hypothesis.

Methoxamine does possess an important antiarrhythmic action. It was apparent early that this action was not due to a carotid sinus vagal reflex from hypertension, since ventricular arrhythmias were abolished,⁹⁷ phenylephrine did not possess the action⁷⁰ and the effect persisted even after section of the vagus.⁷⁰ Recently it has been noted that over 30 chemical analogues of methoxamine also possess antiarrhythmic properties although they do not elevate blood pressure.⁵³ This suggests the existence of a beta-adrenergic receptor blocking effect of methoxamine and its analogues. Indeed, methoxamine and isopropylmethoxamine do possess beta-blocking properties.^{3,51,83,100,117} At first it was thought that this blockade exerted itself only on the metabolic and uterine relaxant properties of beta drugs.¹⁰⁰ It has been established that methoxamine has definite but weak beta-blocking actions on the myocardium.^{83,89} This may explain its antiarrhythmic action. However, Ellis⁵¹ said that he believed that the antiarrhythmic actions of methoxamine were not due to a beta-blocking effect, nor to reflex responses related to changes in

TABLE 1.*—Average Percentage of Contribution of Increments in Venous Resistance to Increments in Total Resistance ($\Delta VR/\Delta TR \times 100$)

| Agent | $\Delta VR/\Delta TR \times 100$ |
|----------------------|----------------------------------|
| Norepinephrine | 13.8 |
| Tyramine | 8.0 |
| Metaraminol | 7.2 |
| Ephedrine | 3.3 |
| Mephentermine | 1.9 |
| Phenylephrine | 1.8 |
| Methoxamine | 1.4 |

*After Zimmerman and coworkers¹⁷⁵.

arterial pressure, nor to changes in refractory period or AV conduction. It was his opinion that the exact mechanism of the antiarrhythmic effect of methoxamine and its congeners remains to be defined.

Polypeptides

Angiotensin II. Angiotensin II is the only major vasopressor agent which is not a sympathomimetic amine. It is an octapeptide composed of a sequence of eight amino acids.¹³² Angiotensin is formed by the proteolytic action of renin, an enzyme normally present in renal tissue, upon renin substrate, a globulin elaborated by the liver. Naturally occurring angiotensin (angiotensin I) is a decapeptide, which is apparently broken down in the blood by the splitting off of two amino acids, to the definitive pressor substance (angiotensin II).

Because of the considerable debate on the inotropic effects of the drug, it is not clear whether angiotensin should be placed in the same functional class as methoxamine and phenylephrine or as metaraminol. Koch-Weser^{90,91} noted a positive inotropic effect on ventricular papillary muscle in kittens, with only slight effect on atrial muscle in cats and no effect on ventricular muscle in frogs. Aviado⁶ said that angiotensin has no inotropic effect. Ross and Braunwald,¹⁴¹ Bianchi¹⁷ and Downing and Sonnenblick⁴³ expressed belief that the drug has little direct influence on ventricular function. Ross and Braunwald¹⁴¹ were able to produce increases in end diastolic pressure with angiotensin in a manner thought to be analogous to methoxamine. Yu and coworkers¹⁷¹ found no change or a slight decrease in cardiac output and stroke volume in man, a significant increase in total systemic and total pulmonary resistance, a significant increase in stroke work of both ventricles, and a significant prolongation of circulation time. The cardiac output is either unchanged or decreased in normal human subjects.^{57,145} Angiotensin exerts a cardioaccelerator action¹²⁶ which is not direct and is probably mediated by the release of extracardiac catecholamines.^{85,94} Berry, Austen and Clark¹⁵ and Fowler and Holmes⁵⁸ noted a biphasic response to infused angiotensin. This response is characterized in dogs by a brief period of negative inotropic effects, followed by a prolonged period of positive inotropic and chronotropic effects. Berry and coworkers¹⁵ went one step further by separating the cardio-

pulmonary and the systemic circulations with two extra-corporeal circuits. The injection of angiotensin into the cardiopulmonary circuit produced only a negative inotropic effect, with no changes in blood pressure or heart rate. Injection in the systemic circuit produced a delayed, sustained increase in myocardial contractile force, heart rate and blood pressure in all animals, with no negative inotropic phase. Following beta-adrenergic blockade, injection of angiotensin into the systemic circuit produced only an increase in systemic blood pressure. No change was noted in ascending aortic pressure, myocardial contractile force or heart rate. These studies indicated a transient direct negative inotropic effect on the myocardium. The investigators believed that the delayed changes in blood pressure, heart rate and myocardial contractile force in intact dogs and after systemic circulatory injection were probably due to the agent's peripheral effect, mediated by sympatho-adrenal discharge.

It is possible that the initial negative inotropic effect of angiotensin, rather than being a direct myocardial effect, was due to a transient period of myocardial hypoxia secondary to coronary vasoconstriction. The analogy in the chemical structure to vasopressin, a well-known coronary constrictor,⁷⁰ suggests that a coronary constricting effect is possible. Johnson and Bruce⁸⁶ found no change in coronary blood flow in three normal human subjects. However, these measurements were made after the initial transient negative inotropic effect noted by Berry and coworkers¹⁵ would have disappeared. Myocardial hypoxia, as well as sympathetically induced positive inotropic action with increase in blood pressure, would be expected to increase coronary flow reflexly. In the completely isolated mammalian heart, Lorber¹⁰⁸ found that angiotensin decreased coronary flow and increased myocardial oxygen consumption. Admittedly these studies were performed before a pure synthetic substance was available. Hence impurities may have been responsible for these results. However, Fowler and Holmes⁵⁸ recently found a coronary vasoconstricting effect of angiotensin in the dog heart-lung preparation, while Meier and coworkers¹¹⁸ have observed the phenomenon during right heart by-pass in cats. These studies suggest that angiotensin should be used with caution—if at all—under most circumstances.

Angiotensin causes a specifically great degree of constriction of the splanchnic bed.^{70,76,161} According to one theory of shock,^{104,161} this constrict-

tion would be detrimental. Lillehei¹⁰⁴ expressed belief that one of the major causes of irreversible shock, at least in dogs, is a decreased flow to the bowel with a subsequent outpouring of endotoxins and loss of plasma into the bowel. The same reasoning is applicable to norepinephrine.

During shock in man, angiotensin produces a significantly lower cardiac output and urinary flow and a disproportionate increase in peripheral resistance when compared with norepinephrine and metaraminol.¹⁶² Hence, both in normal subjects and in patients in shock, the rise in blood pressure is due mainly to an increase in arterial resistance without an effect on venous return or systemic flow. Udhoji and coworkers¹⁶⁴ expressed the opinion that the use of angiotensin should be limited to patients with simple neurogenic hypotension uncomplicated by hypovolemia, in whom a decrease in peripheral resistance may be the primary cause of circulatory failure.

Angiotensin offers two advantages over norepinephrine—it does not cause sloughing when an intravenous infusion leaks into the subcutaneous tissue and it does not cause tachyphylaxis. The latter phenomenon may be due to the pre-capillary constricting effect of angiotensin.⁷⁰ Constriction of this type would not increase capillary pressure as would the post-capillary constriction of norepinephrine. Hence, the loss of plasma would not be so great, nor would the effect of angiotensin upon the circulation be diminished with time.⁴¹

Another synthetic octapeptide, PLV-2 (2-phenylalanine 8-lysine vasopressin), is available only for clinical trial. Because of its striking effects on peripheral vessels and lack of direct effects on the heart, its manufacturers have wisely suggested that its use be restricted to that of a local vasoconstricting agent to decrease toxicity and to prolong the duration of action of certain injected drugs, such as local anesthetics, or to produce local hemostasis.⁷¹ However, PLV-2 raises the possibility of synthesizing other drugs with a more selective vasoconstrictive action. In studies in shocked rats,^{4,116} PLV-2 produced better capillary perfusion and venous return than norepinephrine, angiotensin, and controls. This suggests that it may be possible to synthesize more selective pressor agents. If so, it would be particularly desirable to make postarteriolar perfusion more pressure-dependent than it now is. What we really need is to reduce the capacitance bed without shutting off the flow in any vascular bed.

Mephentermine, Methamphetamine and Hydroxephedrine. These drugs show a predominance of cardiac stimulation over vasoconstriction, probably only at a lower dose level. The latter two agents are usually not used as pressors because of their "side effects" of cortical stimulation. Mephentermine possesses some cortical stimulation,^{48,92} although considerably less than the other two drugs. Andersen and Gravenstein⁵ reported a sense of well-being in three of six normal subjects in whom mephentermine was used as a pressor. I have noticed this same phenomenon in five of six subjects. Ephedrine showed no such effects.

Initially mephentermine was considered to be a vasoconstrictor drug.^{25,80} Later many considered it to exert a mild vasodilating effect.^{7,8} This is one of the bases for its theoretical preference in the treatment of hypotension. However, recent studies in isolated perfused limbs have demonstrated a vasoconstricting action.¹⁵⁸ Li and coworkers¹⁰¹ in studies on normal conscious man found no significant change in total peripheral resistance for the first 20 minutes, although vasoconstriction supervened subsequently. It is possible that the delayed appearance of vasoconstriction was a secondary response, perhaps mediated by a sustained release of catecholamines. Andersen and Gravenstein⁵ found an increase in total peripheral resistance for the first 20 minutes; with a subsequent return to control levels. It is apparent that further studies are required to clear up the discrepancies.

Of considerable importance is the pronounced increase in venous return noted with mephentermine.^{163,167} Isoproterenol, a known cardiac stimulant and vasodilator, is the only other agent studied that possessed this property. Udhoji and coworkers¹⁶⁴ postulated that this could be due either to direct venous constriction or to the opening up of small veins beyond which relatively large quantities of blood may be pooled. The similarity of action of isoproterenol, plus the findings of Zimmerman and his associates¹⁷⁴ (Table 1) indicating that mephentermine is a very poor venoconstrictor, point to the latter explanation. Most of this effect, could arise from a forward push, produced by increased myocardial contractility through mildly constricted arterioles and veins, and into the right atrium. This, of course, is a very efficient way to increase cardiac output and is evidence in favor of mephentermine. Horsley and Eckstein⁸² found a venous constriction in man after administration of mephentermine and concluded that the drug

might produce an increase in cardiac output by extruding blood from the extremities.

It is obvious that many of the differences in observations on peripheral vessels must be due to differences in species, doses, initial conditions and preparations. Li and coworkers¹⁰³ pointed out that in patients with sympathetic block produced by spinal anesthesia, the effects of mephentermine depend upon the state of the cardiovascular system: If the cardiac output is low, the pressor effect is due mainly to an increase in cardiac output; if total peripheral resistance is low, the pressor effect is brought about by an increase in total peripheral resistance. This seems to be a sensible way to produce a pharmacologic effect.

In contrast to the confusion existing on the vasoconstricting properties of mephentermine, no one has disputed its excellent positive inotropic properties. This property has been noted in dogs,* frogs⁶⁷ and man.^{61,68}

Another feature of this fascinating drug is its antiarrhythmic property. Almost invariably a positive inotropic effect and arrhythmogenic effect are associated; mephentermine may be the sole exception. Most of the antiarrhythmic action of mephentermine is due to its effect on the conduction system of the heart—a decreased conduction time in the bundle of His and the Purkinje system, a decreased atrio-ventricular conduction time and a decrease in the refractory period of the atrium.^{128,157} This antiarrhythmic property has been noted in isolated hearts⁶⁶; in certain arrhythmias produced by acetyl strophanthidin in dogs† and in isolated guinea pig atria¹⁵⁶; in arrhythmia produced by ligation of the anterior descending coronary artery in dogs; in spontaneous ventricular fibrillation during hypothermia in dogs³⁴; in nodal rhythms, supraventricular tachycardia, bigemini and premature ventricular beats in man^{13,169}; and in the arrhythmia accompanying the shock of myocardial infarction.¹⁴ However, it has shown no protective effect against arrhythmia caused by a combination of cyclopropane and epinephrine.^{50,111} One group claims that mephentermine can actually produce arrhythmia during cyclopropane anesthesia in dogs,⁴⁰ another that mephentermine induces ectopic foci, abnormal beats and abnormal responses to test stimuli in dogs.⁶⁵ Gilbert and coworkers⁶⁴ also detected a moderate increase in irritability to multiple stimuli. However, they also noted this tendency with methoxamine, which no

one disputes is an antiarrhythmic drug. In one series, mephentermine could not protect against ventricular fibrillation induced by manipulation of the heart during hypothermia.³⁵

Reconciliation

From all this conflicting mass of data on pressor drugs, what can be said about the therapeutic use of pressors, both present and future? This, after all, for the clinician is the ultimate goal of research. It appears that vasopressors are a last resort for the treatment of most types of hypotension. However, in the evaluation of the material presented here and the conclusions drawn from it, it should be remembered that much of this information is quite recent and, therefore, comes during a period when the therapeutic cycle has swung against pressor agents. Scientific papers, like ladies' hats, tend to follow a style.

Nevertheless, a few suggestions are in order. Do not treat the blood pressure—treat the patient. If a patient's blood pressure is low, but he is warm, dry, fully conscious and rational, has no chest pain or electrocardiographic changes, and is producing urine, then raising the blood pressure is obviously not mandatory. If treatment is necessary, correcting the underlying cause of the hypotension should be done before merely correcting a symptom. If shock is caused by hypovolemia, replace blood volume. Hemorrhagic, endotoxic, septic and burn shock are often accompanied by an enormous loss of plasma⁶⁹ and/or extracellular fluid¹⁵¹—replace it. If in the anesthetized patient the anesthesia is too deep, lighten it. Often hypotension accompanied by pronounced bradycardia can be corrected by atropine 0.5 mg administered intravenously.⁴⁹ (This may be dangerous during cyclopropane anesthesia.)* The hypotension due to spinal anesthesia or “neurogenic” shock can often be reversed simply by elevating the legs. This may increase venous return and cardiac output as much as 700 ml²⁶ per minute.

In certain cases of shock, all therapeutic measures seem to be of no avail. Pressor agents may actually worsen the situation.^{59,104,105,125} In these cases one should make every effort to find a hidden cause for the “refractory” hypotension¹⁵⁴ such as hypoxia, acidosis or, particularly, continued hemorrhage. In many cases, shock may respond to what at first would seem to be the opposite of the principle initially stated—treat the cause of any

*Reference Nos. 54, 55, 63, 67, 120, 168.

†Reference Nos. 127, 129, 136, 156.

*Reference Nos. 33, 84, 87, 88, 134.

pathologic condition. However, the cause of the refractory state may not be hypotension *per se* but, rather, poor tissue perfusion.⁷⁹ Thus, the use of vasodilator therapy during shock has been suggested and studied for the past several years.* The present review is not intended to evaluate this therapy. The reader should consult the excellent reviews by Lillehei,¹⁰⁵ Nickerson¹²⁵ and Udhoji.¹⁶⁴ Steroids have been studied in the therapy of shock.^{105,144,164} The doses needed are far above any replacement needs. Therefore, this should be considered a pharmacologic effect of the steroids, rather than mere replacement.

If it is decided to use a pressor drug, it should be used sparingly, briefly, and never to return blood pressure to the patient's "normal" levels. It is probable that few vasopressors will harm the patient if used for *less than 15 minutes*. They should be used only as a temporary measure, while diagnostic and other therapeutic measures are being taken. To elevate a patient's blood pressure with a pressor agent and then to walk away with a sense of security without making further efforts is unforgivable.

Which pressors should one use? This depends entirely upon the circumstances, of course. Mephentermine or ephedrine would seem to be good initial trial drugs to use in most cases. A drug which raises total peripheral resistance and increases myocardial contractility and venous return, such as ephedrine or mephentermine, would be a good choice for the hypotension occurring during spinal anesthesia or general anesthesia. Raising the total peripheral resistance of patients in hypovolemic shock (from hemorrhage, burns and intestinal obstruction for example) has no salutary effect until blood, plasma or extracellular fluid volume is replaced; then the pressors are usually not necessary. Methoxamine, angiotensin and phenylephrine would appear to have few, if any, uses. If it is absolutely essential to raise blood pressure immediately because of obvious myocardial or cerebral insufficiency, then metaraminol or norepinephrine are quite dependable in elevating blood pressure.

The treatment of shock following acute myocardial infarction is a separate problem. In shock of this type, elevation of blood pressure with pressor drugs has not significantly altered the mortality rate.^{18,37,150} Bloch and coworkers²⁰ studied cardiogenic shock induced in dogs by coronary micro-

emboli. Survival was greatest in those dogs in whom peripheral resistance was lowered by alpha-adrenergic blockade; lowest in those dogs in whom peripheral resistance was increased with norepinephrine. The combination of alpha blockade and norepinephrine improved performance, but did not increase survival above that from alpha block alone. They felt that maintenance of normal circulatory function with decreased cardiac oxygen consumption was responsible for the better survival rate. Another new approach to this problem may be the use of beta-blocking drugs. The use of these drugs might have two effects. First they produce an antiarrhythmic effect. Arrhythmia is known to be a major killer in the acute period of myocardial infarction. Second, they may correct the intense vasodilation occurring during *some* but probably very few cases of myocardial infarction. Vasodilation may result from an over-activation of the beta-adrenergic receptors. Preliminary studies^{110,155} have shown success with this form of therapy. This is a potentially dangerous maneuver, and should be evaluated thoroughly before it is accepted.

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CASE REPORTS

Myiasis of the Foot Caused by *Phaenicia Sericata* (Meigen)

W. PETER HOREN, M.S., *San Francisco*

THIS PAPER DESCRIBES a case of localized myiasis in a human, a condition caused by the invasion of the body by fly larvae. The several clinical types vary with the site of the infestation and the species of fly, the commonest in the United States being *Cochliomyia homnivorax*, *Sarcophaga* species, and *Wohlfartia vigil*. Wound myiasis is rare,⁹ and myiasis caused by the greenbottle fly, *Phaenicia sericata* (Meigen), the infecting agent in this case, is also infrequent.^{2-3,6-9} Only five cases in humans have been reported from North America in the past 20 years, but myiasis caused by this fly is common in animals. It is believed to occur occasionally (unreported) in man in the Sacramento area.⁵

The gravid female usually lays an egg mass on or near odorous sores or the soiled wool of animals. Sometimes several females deposit their eggs, numbering thousands, as an aggregate mass. The common breeding medium is carrion, but garbage and manure are occasional alternatives. The larval feeding period varies from one and a half to nine and a half days. Mature larvae leave the lesion where they are feeding for pupation, which usually takes place on soil. Pupation may be postponed several months under unfavorable condi-

tions, and hibernation usually takes place in the larval stage. When breeding is continuous, eight generations may develop in a year. Young larvae feed at the surface of a lesion, older larvae bore deeply into healthy tissue and may produce serious wound myiasis. Nevertheless, *P. sericata* was formerly the most common fly species used in larval form for wound therapy.⁴

Report of a Case

A 68-year-old white man with previous history of arteriosclerosis obliterans of the left superficial femoral artery was readmitted to the University of California Medical Center in June 1965. On examination of his left foot extensive necrosis of the first, third and fourth toes was noted (Figure 1). Between the toes were several deep, odorless, aseptic ulcers in which many active fly larvae were readily seen (Figure 2). On removal of the maggots, tendons of the foot were visible. The author removed seven of the maggots, which were reared on ground beef to the adult stage for specific identification. The adults were sent to Mr. Benjamin Keh, Bureau of Vector Control, California State



Figure 1.—Left foot, showing necrotic first, third and fourth toes. Larvae of *Phaenicia sericata* are visible between the third and fourth toes.

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Submitted 12 December 1966.

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Figure 2.—Enlargement showing several larvae in the ulcer between the third and fourth toes. Spiracular plates on the posterior ends of two larvae are readily visible (arrows).

Department of Public Health, Berkeley, who identified them as *Phaenicia sericata* (Meigen). The larvae remaining in the ulcer were killed with a chloroform-soaked wad of sterile absorbent cotton applied to the surface. (Irrigation with a solution of chloroform and milk has also been recommended.¹) A total of 63 larvae were removed from the wound. Local treatment consisted of a sterile dressing for the lesion and analgesics given orally.

Evidently the patient's habit of lounging barefoot on the porch of his sister's rural home in Sonoma County exposed him to the flies, and the gangrenous condition of his left foot attracted gravid females, which oviposited on the necrotic tissues.

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Renal Carcinoma as an Accidental Finding on Needle Biopsy

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IT IS COMMON medical knowledge that carcinoma of the kidney is frequently an insidious and silent condition. Hematuria occurs as the first or one of the first complaints in only 60 per cent of cases, a mass in 40 per cent, pain in 50 per cent and the classic triad of a mass, pain and hematuria in only 15 per cent of patients.⁹ Even pyelographic changes secondary to kidney tumors of moderate size are not always reliable, and findings in the urine of abnormal sediment or enzymes are usually manifestations of locally extensive malignant disease. The case here reported is unique in that a minute renal cell tumor was found accidentally on needle biopsy.

Report of a Case

A 29-year-old Caucasian lawyer was found to have microscopic hematuria on a routine physical examination in 1962. An intravenous urogram at that time was interpreted as normal. There was

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Submitted 19 December 1966.

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a strong family pattern of "familial nephritis," three brothers having died of "glomerulonephritis" at ages 25, 28 and 30. Two brothers, aged 40 and 42, were living but they too had asymptomatic hematuria. One maternal male cousin and a paternal male cousin had nephritis; another paternal male cousin had kidney disease diagnosed as pyelonephritis. None of the brothers was deaf. In May 1964 the patient was examined as a possible kidney donor for a brother who was dying of terminal renal failure, and once again was found to have microhematuria and also 2 plus proteinuria. Because of suspected "familial nephritis" a percutaneous biopsy of the right kidney was performed. One cylinder of tissue was removed with the Franklin VIM-Silverman needle. The biopsy showed clear cell carcinoma of the kidney (Figure 1).

After the histologic diagnosis of clear cell carcinoma was reported, another intravenous urogram was made which again failed to disclose any abnormality of the renal contours or collecting systems. Selective renal angiography disclosed a 2 cm lesion in the lower pole of the right kidney, seen best in oblique views (Figures 2 and 3). The tumor had the vascular staining characteristic of renal carcinoma.

The patient's blood pressure was 120/80 mm of mercury. The abdomen was soft without masses. The hematocrit was 43.5 per cent, and hemoglobin was 15.6 gm per 100 ml of blood. The urine was a clear yellow with specific gravity of 1.011, 30 mg of protein per 100 ml and 1 to 2 erythrocytes and 2 to 3 leukocytes per high power field. Serum

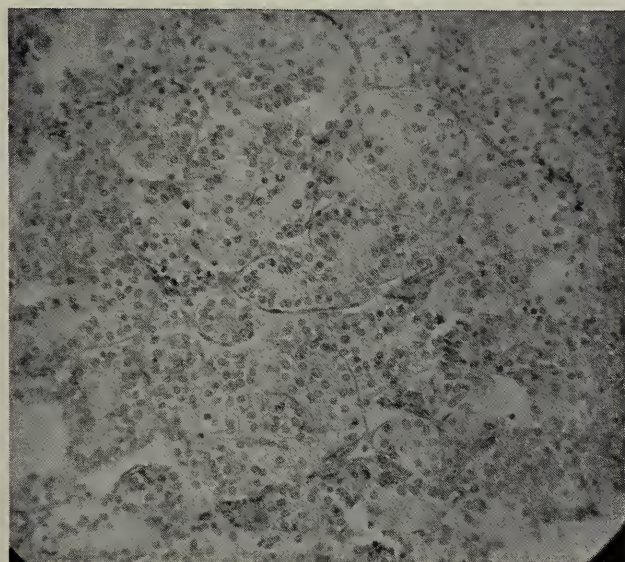


Figure 1.—Photomicrograph of needle biopsy specimen showing clear cell carcinoma ($\times 150$).

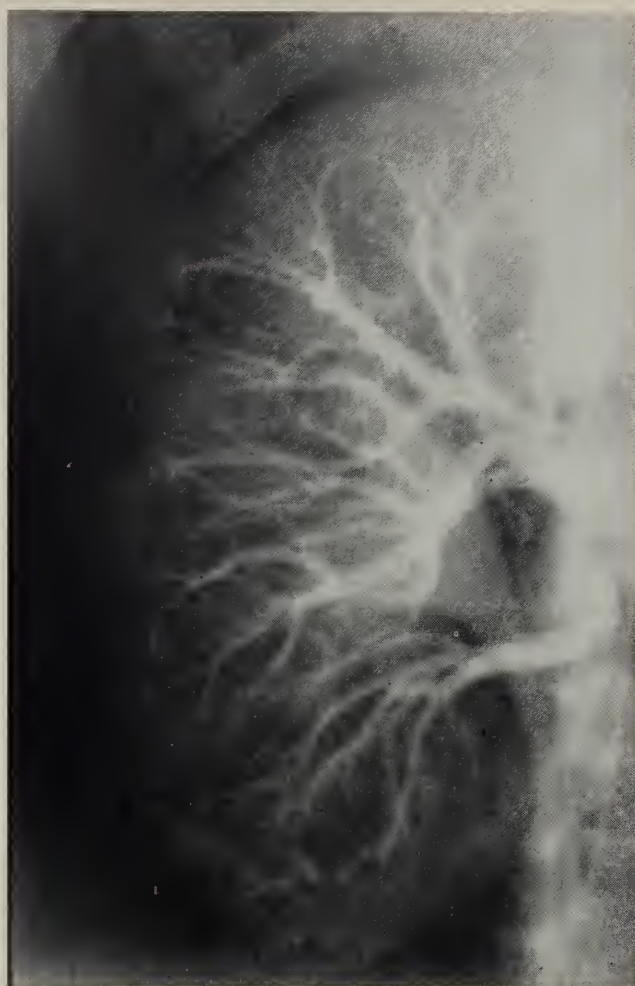


Figure 2.—Selective right renal arteriogram showing pooling of contrast in the small tumor at the lower pole of the kidney.

creatinine was 0.7 mg and fasting blood sugar 90 mg per 100 ml. Cystoscopy and retrograde pyeloureterography disclosed no abnormalities.

An incision was made through the right flank and the tumor was found on the surface of the right kidney at the lower pole, where it was slightly adherent to overlying perinephric fat. After the kidney had been mobilized and the renal artery had been temporarily clamped, the lower pole of the kidney was resected. About one-tenth of the kidney mass was removed with a good margin of renal tissue about the tumor (Figure 4). Gerota's capsule and perinephric fat were removed where they were adherent to the lower pole, presumably as the result of previous needle biopsy. There was no evidence of tumor in lymph nodes adjacent to the kidney.

The pathologist reported that the portion of kidney removed weighed 12 grams and measured $4 \times 4 \times 3$ cm. The tumor was approximately 1.6 cm in diameter and was of yellow gray appearance



Figure 3.—Nephrographic phase, oblique view of right renal arteriogram showing tumor at the lower pole.

with some hemorrhagic areas. On microscopic examination the cortical lesion was seen to be pseudoencapsulated and to consist of sheets and cords of cells arranged in a glandular fashion. The cells had large round nuclei and clear cytoplasm, although some of them were completely vacuolated. No vascular invasion was found. The tumor was diagnosed as a cortical adenoma by one pathologist, on the basis of its size alone. The sections of remaining "normal" kidney showed rare foci of centrilobular proliferation and basement membrane thickening. The diagnosis was minimal focal glomerulonephritis.

Discussion

Small solitary renal tumors are not infrequently found at autopsy. Uys¹ reported incidences ranging from 0.3 to 3.9 per cent. Björnberg⁴ found 14 unsuspected renal carcinomas in an autopsy series of 33 cases of hypernephroma. Böttiger and co-workers^{5,6} detected 89 cases of renal carcinoma in 4,560 postmortem examinations; 47 or 53 per cent

of these were accidental findings and in 42 cases the tumor was the cause of death. In six of the cases in which the tumor was found accidentally, the lesion was approximately 3.5 mm in diameter, in ten cases 15 mm, in 13 cases 30 mm, in six cases 50 mm and in 12 cases more than 50 mm. Metastasis had occurred in only one instance—from one of the 30 mm tumors. Bunge and Kraushaar⁷ diagnosed a renal carcinoma 77 mm in diameter. The patient complained of flank pain and was found to have renal microhematuria. Urine from the left kidney showed abnormal cells, and despite a normal appearing retrograde pyelogram, nephrectomy was carried out. The tumor was infiltrative and was diagnosed as a mixture of "hypernephroma and renal cell carcinoma." It was interpreted as a malignant neoplasm of the renal epithelium and therefore was classified as adenocarcinoma of the kidney.

In the case here reported, its lesion was diagnosed as renal cell carcinoma by the pathologist who examined the biopsy specimen (before the gross size of the tumor was known). Showing vascular "laking," the angiographic appearance of the tumor was characteristic of renal cell carcinoma. In sections of the tumor removed at operation, clear cells arranged in tubular form were observed, a histologic picture indistinguishable from adenocarcinoma. The only source of difference between the pathologist who examined the biopsy specimen and the one who reported on the operative specimens was the gross size of the tumor, which influenced one pathologist to designate it as an adenoma.

Although these small tumors are considered by some pathologists to represent benign adenomas, majority opinion^{1,3,13} holds that no histologic distinction can be made between adenomas and small

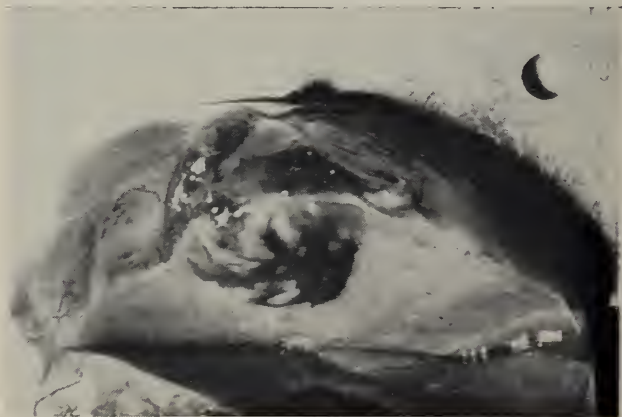


Figure 4.—Gross appearance of surgical specimen showing tumor and generous margin of kidney tissue.

carcinomas. The principal reason for the distinction between adenomas and adenocarcinomas of the kidney on the basis of size derives from Bell's statement that "tumors under 3 cm in diameter have rarely formed metastases."³ Admittedly, this pathologic distinction is an arbitrary one and no consonant opinion exists among pathologists. Certainly all adenocarcinomas begin as small tumors, and since microscopically adenomas and adenocarcinomas are generally indistinguishable, it is perhaps logical that distinctions are made on the basis of the stage of growth alone.

In the present case, therapy was partial nephrectomy, which, considering the size of the tumor and its pseudoencapsulation, appeared to be adequate treatment. Vermooten advocated partial nephrectomy for clear cell carcinoma.¹² Conservation of as much renal tissue as possible was strongly indicated in the present case, particularly in light of the finding of focal glomerulonephritis in the remaining kidney.

The patient and his siblings resemble those with hereditary chronic nephritis previously reported.^{2,8,10} Neither the patient nor his siblings manifested extrarenal abnormalities of the kind seen in some patients with hereditary chronic nephritis—nerve deafness or abnormalities of the eyes, skin or bone. The pathologic features in this case were consistent with early forms of the disorder in showing minor nonspecific changes such as hyalinized glomeruli. Lipid-filled foam cells in the interstitium between the tubules near the corticomedullary junction were not seen. A review of the literature, however, disclosed that the histologic picture of familial nephritis is not consistent and that some patients have had typical interstitial pyelonephritis whereas others have had glomerular crescents and hypercellularity.¹⁰

Summary

A case of early carcinoma of the kidney was detected accidentally on needle biopsy in the study of a patient with familial nephritis. The lesion, 1.2 cm in diameter, was a solitary one in the lower pole of the kidney. The lesion was confirmed by angiography which revealed a characteristic vascular tumor pattern. Treatment was lower pole nephrectomy. Microscopically the tumor was an adenocarcinoma of the kidney, although on the basis of size alone some pathologists would classify it as an adenoma.

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Hemorrhage from The Gallbladder

A Report of Three Cases

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NONTRAUMATIC HEMORRHAGE from the gallbladder (hemorrhagic cholecystitis) is a rare complication of biliary tract disease. Since in signs and symptoms it may mimic several other diseases, the diagnosis is often delayed and is usually not made until operation or autopsy. The symptoms usually resemble those of acute cholecystitis, although the primary diagnosis may be massive upper gastrointestinal bleeding, hydrops of the gallbladder,

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Submitted 12 December 1966.

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hemoperitoneum or obstruction of the common duct.

Few cases of nontraumatic hemorrhage from the gallbladder have been reported. In 1961, Fitzpatrick² reviewed the literature on hemocholecysts (nontraumatic hemorrhage from the gallbladder without free intraperitoneal rupture), and collected 34 cases, while adding one of his own. In 1961 Raycroft and Mastrangelo⁵ reviewed the literature on massive intraperitoneal hemorrhage as a complication of gallbladder disease; they found 16 somewhat similar cases and added two of their own. Our recent experience with three cases of hemorrhage from the gallbladder prompted a further review of the subject and the following case reports.

Reports of Cases

CASE 1.—A 58-year-old white man entered San Francisco General Hospital 1 April 1965 with a one-week history of progressive pain in the right upper quadrant of the abdomen, nausea, and vomiting of clear, yellowish material. He had no recent history of trauma, hematemesis or melena. In 1955 he was told that he had cirrhosis of the liver, and he had a bleeding peptic ulcer in 1959. The temperature was 39.0°C (102.2°F). The right upper quadrant of the abdomen was tender and a large, somewhat tense mass measuring 8 by 10 by 10 cm was palpable as well as visible. Rectal examination was normal and the stool guaiac test was negative for blood. Leukocytes numbered 5,500 per cu mm of blood and the hematocrit was 43 per cent. Prothrombin time was 64 per cent. A plain roentgenogram of the abdomen showed multiple calculi in the right upper quadrant in what appeared to be a large, distended gallbladder.¹ After conservative treatment the patient rapidly became asymptomatic and within eight hours after admission the mass was no longer palpable. However, the mass reappeared 36 hours later, and symptoms became worse. Surgical intervention was then considered mandatory. At operation the gallbladder was large, distended, edematous and inflamed. On aspiration, 750 ml of blood, dark at first and then bright red, was withdrawn. When the gallbladder was opened, the entire mucosa appeared to be bleeding. Multiple calculi were found, including an impacted cystic duct stone. Cholecystectomy was performed. During operative cholangiography, clear golden bile was obtained from a normal-appearing common duct. Postoper-

atively the patient was transiently icteric. On the fourth postoperative day, he passed a black tarry stool which was guaiac-positive. Gastric aspirate was guaiac-negative. Recovery then was satisfactory.

Pathologic examination of the gallbladder showed acute hemorrhagic cholecystitis. The wall was thickened and acutely inflamed in all layers. Hemorrhage and edema of the submucosa, with sloughing of the mucosa, were present.

Comment: Acute hemorrhagic cholecystitis manifested itself as rapidly recurring hydrops, prompting surgical intervention.

CASE 2.—An 82-year-old white man was admitted to the San Francisco General Hospital 15 October 1964 with a 12-hour history of upper abdominal pain, and vomiting of "coffee grounds" material. He was disoriented and a more extensive history could not be obtained. Blood pressure was 88/55 mm of mercury and the pulse was 128. The abdomen was slightly distended and a fluid wave was present. Leukocytes numbered 14,200 per cu mm of blood, and the hematocrit was 46 per cent. A plain roentgenogram of the abdomen showed no abnormality. Paracentesis yielded large quantities of bloody fluid. At laparotomy approximately 1,000 ml of bloody fluid was present in the peritoneal cavity. The gallbladder was acutely inflamed and gangrenous and had a perforation 2 cm long, which was bleeding briskly. The diffuse bleeding appeared to come from the entire mucosa. Cholelithiasis was also present. The stomach and duodenum were normal. Cholecystectomy was performed. Postoperatively, the patient did well at first but his condition gradually deteriorated and nine days after operation he died of pulmonary complications.

Comment: Acute hemorrhagic cholecystitis, an unusual cause of hemoperitoneum, was controlled by cholecystectomy.

CASE 3.—A 55-year-old white man was admitted to the San Francisco General Hospital 20 September 1965 with a three-day history of nausea, vomiting and generalized abdominal pain. He had a past history of severe claudication of the lower extremities. Aorto-iliac thromboendarterectomy had been performed in June 1965. The temperature was 38.5°C (101.3°F). The entire abdomen was rigid and pronounced guarding was evident in all quadrants. Bowel sounds were hypoa-

blood and the hematocrit was 36 per cent. Roentgenograms of the abdomen showed dilated loops of small bowel and right colon, which contained air-fluid levels. Nasogastric aspirate and stool were positive for occult blood. The preoperative diagnosis was superior mesenteric artery occlusion. At laparotomy, no abnormality was found in the small bowel, but approximately 300 ml of dark, viscous blood was seen in the infrahepatic space. The gallbladder was greatly dilated and hemorrhagic; a recent perforation was noted in the posterior portion of the cystic ampulla. Several cholesterol stones measuring 3 to 4 mm were floating free in the pericholecystic area. Cholecystectomy was carried out. The postoperative course was uneventful. Microscopic examination of the gallbladder showed hemorrhagic material within the lumen and considerable amounts of extravasated blood dissecting through the gallbladder wall.

Comment: Acute hemorrhagic cholecystitis mimicked superior mesenteric vascular occlusion, with gastrointestinal bleeding. Hemobilia caused anemia, free-peritoneal bleeding and occult blood in stools and nasogastric aspirate.

Discussion

Bleeding, an infrequent complication of gallbladder disease, is usually caused by gallstones.² Acute hemorrhagic cholecystitis was associated with cholelithiasis in all three of the cases here reported. The wide variety of presenting symptoms often delays the correct diagnosis.^{3,4,6} In Case 1, the rapidly reappearing hydrops might have alerted us to hemorrhage into the gallbladder. As the gallbladder initially distended, the stone in the cystic duct apparently became disimpacted and the gallbladder decompressed as blood passed into the bowel through the common duct. Later, a stone probably again became impacted and the mass reappeared. The fact that the patient passed a tarry stool on the fourth postoperative day further confirms this impression.

The combination of hemoperitoneum and peritonitis usually results from perforated and bleeding duodenal ulcers. Hemoperitoneum as a complication of gallbladder disease is usually due to erosion of the cystic artery or one of its branches, or

to an area of focal necrosis at the site of perforation.⁵ In Case 2 a perforation was found, but the mucosa of the gallbladder appeared to be oozing blood from its entire surface. Cholecystectomy effectively controlled the hemorrhage. The patient died later of pulmonary complications.

In Case 3, both hemoperitoneum and evidence of gastrointestinal blood loss were found. Gross bleeding had occurred into the lumen of the gallbladder, and before perforation the organ had decompressed by way of the cystic duct into the duodenum. Extravasation of blood was found in all layers of the acutely inflamed gallbladder, which was also the site of acute cholecystitis.

In other reported cases of acute hemorrhagic cholecystitis with hemobilia, gastrointestinal blood loss was severe enough to warrant exploratory laparotomy because of a presumed diagnosis of hemorrhaging duodenal ulcer.^{1,3} Since the gallbladder may be a source of enteric as well as intraperitoneal blood loss, hemorrhage can usually be treated successfully by prompt operative intervention.

Summary

Three cases of hemorrhagic cholecystitis with different clinical manifestations are described. One patient had acute cholecystitis with recurrent hydrops, another had hemoperitoneum and the third had hemoperitoneum with gastrointestinal bleeding. Cholecystectomy successfully controlled the hemorrhage in all cases. The biliary tract should be considered as a possible source of bleeding in patients with obscure hemoperitoneum and upper gastrointestinal hemorrhage.

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Hypercalcemia of Malignant Disease

These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California Medical Center, San Francisco. Taken from transcriptions, they are prepared by Drs. Martin J. Cline and Hibbard E. Williams, Assistant Professors of Medicine, under the direction of Dr. Lloyd H. Smith, Jr., Professor of Medicine and Chairman of the Department of Medicine.

DR. SMITH*: For our Medical Grand Rounds this morning, we are presenting two quite different types of endocrine tumors. The patient to be discussed first was referred to the hospital by a physician in Northern California.

DR. QUILICI*¹: The patient, a Caucasian man 67 years of age, entered an outside hospital three months ago because of aching in his joints, loss of weight, loss of energy and severe lower back pain of about one year's duration. He also complained of wheezing and mild intermittent inability to swallow. On physical examination pronounced clubbing of both the fingers and the toes was noted. An x-ray film of the chest was reported to show elevation of the left diaphragm. An upper gastrointestinal series was within normal limits. The result of a latex fixation test was positive. A presumptive diagnosis of rheumatoid arthritis was made and the patient was treated with salicylates.

A month later the patient reentered the same hospital with similar complaints. He had lost approximately 50 pounds. Because of fever to 39.4°C (103°F) and progressive disorientation he was transferred to the University of California hospital 25 days ago. He was unable to give any history at the time of admission.

On entering this hospital he appeared to be both acutely and chronically ill and was mentally dull. He had mild respiratory distress and appeared to be dehydrated. The temperature was 39°C, respirations were 30 per minute and blood pressure

120/70 mm of mercury. Results of examination of the head, eyes, ears, nose and throat were within normal limits. A grade II/VI apical systolic murmur was heard. There were mild supraclavicular and suprasternal retractions and intercostal retractions over the left hemithorax. The breath sounds were absent over the entire left side of the chest. Tenderness was noted in the right upper quadrant of the abdomen. Neurological examination revealed stupor but no localized neurological abnormalities. On examination of the extremities pronounced clubbing both of fingers and toes was noted. There was no evidence of arthritis.

The laboratory data were as follows: Hemoglobin 11.4 gm per 100 ml, leukocytes 13,700 per cu mm of blood with cell differential within normal limits and sedimentation rate 52 mm in one hour. The urine sediment contained many white cells per high power field. Serum sodium was 130 mEq, carbon dioxide 24.1 mEq and chloride 86.5 mEq per liter. Serum creatinine was 1.8 mg and serum protein 7.1 gm per 100 ml; and serum electrophoresis demonstrated 41 per cent albumin and 20 per cent alpha-2-globulin. An electrocardiogram was within normal limits. The plasma cortisol level was 22.4 mcg (normal 10 to 20 mcg), serum calcium 13.1 mg and serum phosphorus 3.8 mg per 100 ml. Alkaline phosphatase was 2 Shinowara-Jones-Reinhardt units. Calcium content of a 24-hour specimen of urine was 50 mg. No cells were present in the spinal fluid and the protein content was 40 mg per 100 ml. Microscopic examination of sputum showed numerous Gram-positive cocci, and cultures of the sputum

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*¹John Quilici, M.D., Resident in Medicine.

grew *Staphylococcus aureus* sensitive to all antibiotics tested.

Initially the patient was treated with intravenous fluids, penicillin and nasotracheal suctioning. On the morning after entering the hospital he was more coherent and the stupor was less pronounced. By the morning of the second hospital day he was again semicomatose. At this time the serum calcium level was 14.2 mg per 100 ml. Over the next 12-hour period he was given intravenously 1 liter of 0.15 molar sodium phosphate. The following morning the serum calcium had decreased to 9.2 mg per 100 ml with a concomitant transient elevation of the serum phosphorous level. The patient's mental status was somewhat improved. Because of roentgenographic evidence of increasing atelectasis of the left lower lobe and the possibility of a tumor in this area, bronchoscopic examination was done on the third hospital day. This showed a stenotic lesion at the orifice of the left lower lobe. Biopsy of a specimen taken at this time was negative for cancer, but bronchial washings were interpreted as class 5, which is diagnostic of malignant disease. Later that day the patient became acutely dyspneic. He was treated with high doses of penicillin and chloramphenicol and 300 to 600 mg of hydrocortisone per day. The latter drug was given for two reasons: (1) The possibility of adrenal insufficiency was considered although a blood cortisol level drawn before cortisol infusion proved to be normal; and (2) to lower serum calcium. Despite these measures he died on the sixth hospital day.

DR. RUSSELL*²: The x-ray film of the chest on admission demonstrated pronounced loss of volume on the left. There was almost complete atelectasis of the left lower lobe and a hilar mass. This was confirmed in the lateral view.

DR. SMITH: The postmortem findings will be summarized by Dr. George Bailey of the Pathology Department.

DR. BAILEY*³: At the time of autopsy a large tumor was found in the left lower mainstem bronchus, completely obstructing the bronchus as well as the vasculature to the left lower lobe. The tumor had the pattern of an adenocarcinoma forming glandlike structures. Other evidence of this tumor was found in the adrenal glands, which weighed

approximately 30 grams each compared with a normal weight of approximately 5 grams.

DR. SMITH: This particular patient exhibits a number of extra-pulmonary manifestations of carcinoma of the lung which could be discussed. Perhaps the most striking metabolic manifestation was that of hypercalcemia. We are particularly fortunate that Dr. Gilbert Gordan, one of the leading authorities on hypercalcemia of malignant disease, is here to open the discussion. He has made some very important recent contributions to our understanding of the pathogenesis of the hypercalcemia associated with cancer, particularly that which may occur with carcinoma of the breast.

DR. GORDAN*⁴: The House Staff has been extremely kind to me in preparing the protocol for this case. My first reaction on reading the case history was that this was a typical example of the pseudohypercalcemia of adrenal insufficiency. It was of the right magnitude—about 14 mg per 100 ml—and the patient had low serum sodium, high potassium and the kind of tumor which often invades the adrenal glands. I was, therefore, completely convinced and prepared to discuss this subject when I was informed that the patient's plasma cortisol level, before the administration of corticoids, was 22 mcg per 100 ml. Obviously if this information had been presented after my discussion, it would have been most embarrassing.

I think in the hypercalcemia of malignancy one must consider four possible mechanisms: (1) Direct lysis of bone by metastasis; (2) Secretion by the tumor of parathyroid peptide; (3) Secretion by the tumor of the osteolytic sterol we have recently found in human breast cancer; and (4) Adrenal insufficiency secondary to metastasis.

For reasons which quickly become apparent I think we can exclude parathyroid hormone secretion: The serum phosphate level was normal; the tubular reabsorption of phosphate (TRP) is impossible to evaluate since he had a glomerular filtration rate of only 36 ml per minute which uniformly lowers TRP. We have no information about sterol levels in this patient, and we can hardly blame adrenal insufficiency if the plasma cortisol level was truly 22.4 mcg per 100 ml. In trying to decide between metastatic lysis and humoral osteolysis, it will be necessary to review the evidence for the latter.

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*³George Bailey, M.D., Resident in Pathology Department.

*⁴Gilbert S. Gordan, M.D., Professor of Medicine.

This patient was one of two who were on the ward at the same time with hypercalcemia of malignancy. Hypercalcemia is probably the most common of the specific metabolic complications of malignant disease. Currently, there is great interest in these complications, for they point to some of the ways cancers harm their victims. Sometimes, too, they may be the very first manifestations of the underlying tumor.

Table 1 lists seven reasonably well-documented para-endocrine syndromes in which tumors elaborate hormones or other humoral factors inappropriate for the tissue from which the tumor originates.⁴ (I am not referring here to the secretion of appropriate humors such as serotonin by tumors of the respiratory or gastrointestinal tracts). The astonishing feature of this list is the ectopic formation of immunologically and chemically authentic corticotropin (ACTH) by bronchogenic carcinoma or malignant thymoma, and parathyroid peptide by tumors of the lung, kidney or colon. The most versatile of these tumors is the relatively uncommon anaplastic or oat-cell tumor of the bronchus which has been incriminated in producing ACTH, antidiuretic hormone, parathyroid hormone, serotonin and perhaps sponging up insulin and glucagon.

You will note that I have divided the hypercalcemias of malignancy into two groups: One with a low serum phosphate level, now shown to result from ectopic elaboration of parathyroid peptide, and a much commoner one in which serum phosphate levels are normal or elevated.

The first syndrome, hypercalcemia with hypophosphatemia, is of special interest. It has been best established in patients in whom osseous metas-

tatic lesions were few or even could not be found at all. That the tumor itself might secrete parathyroid hormone was first suggested by Albright in 1941.¹ That was in the case of a 50-year-old Greek bootblack who had a carcinoma of the right kidney with a single metastatic lesion in the ilium. He had hypercalcemia and hypophosphatemia but at operation and autopsy, the parathyroid glands appeared normal. The chemical abnormalities disappeared after x-ray treatment to the metastatic lesion and returned preterminally. Albright had the wit and originality to realize that, while erosion of bone by the metastatic lesion might raise the serum calcium, it could not explain a low serum phosphate level; in fact, bone breakdown liberates phosphate into the blood. Since parathyroid hormone lowers the serum phosphate by wasting it in the urine, this hormone seemed likely to have caused both the hypercalcemia and hypophosphatemia. This brilliant hypothesis was confirmed a quarter of a century later when Tashjian and Munson¹⁶ at Harvard identified large amounts of parathyroid peptide by complement fixation in extracts of tumors associated with hypercalcemia, hypophosphatemia without evident bone metastasis. More recently, Berson and Yalow³ have shown excessive amounts of parathyroid hormone in the blood of patients with bronchogenic carcinoma by their highly sensitive and specific radioimmunoassay.

In contrast to the relatively rare syndrome of hypercalcemia with hypophosphatemia, hypercalcemia with a normal or elevated serum phosphate level is very common. It is found in virtually all forms of malignant disease—by far most often in carcinoma of the breast, two-thirds of all cases of hypercalcemia of malignancy being associated with

TABLE 1.—*Para-Endocrine Syndromes*

| <i>Syndrome</i> | <i>Hormone</i> | <i>Tumor</i> |
|-----------------------------------------------|-------------------------|------------------------------------------------------------------|
| 1. Cushing's | ACTH | Carcinoma lung; thymoma; pancreas; etc. |
| 2. Hyponatremia | Antidiuretic hormone | Carcinoma lung |
| 3. Hypercalcemia | | |
| a. low serum phosphate | Parathyroid peptide | Carcinoma of lung, kidney; etc. |
| b. normal serum phosphate.. | Sterol | Breast cancer; etc. |
| 4. Polycythemia | Erythropoietin | Renal tumor or cyst; cerebellar hemangioblastoma; etc. |
| | Unknown | Uterine fibroid |
| 5. Hypoglycemia | Unknown | Hepatoma; adrenal cortical carcinoma; large fibromas or sarcomas |
| 6. Precocious puberty or gynecomastia | Chorionic gonadotrophin | Hepatoma; adrenal cortical carcinoma; etc. |
| 7. Chemical or clinical hyperthyroidism | Thyrotrophin (?) | Chorionic carcinoma; mole; testis tumor |

TABLE 2.—Serum and Urine Calcium and Phosphate Levels in Patients with Breast Cancer

| Subject | Serum Calcium (mg/100 ml) | Serum Phosphate (mg/100 ml) | Tubular Reabsorption (Per Cent) | |
|--------------------------------------|------------------------------|--------------------------------|---------------------------------|--------------|
| | | | Calcium | Phosphorus |
| 32 Normal women..... | 10.40 ±0.08 | 3.5 ±0.07 | 97.8 ±0.3 | 85.0 ±0.5 |
| 50 Breast cancer, untreated | 10.68 ±0.08 | 4.0* ±0.03 | 98.0 ±0.16 | 85.4 ±0.8 |

*=P <0.01, compared with normal.

such lesions. In most, but not all, of these cases, osteolytic metastasis is present and usually widespread. Our data⁸ agree with those of Jessiman and coworkers¹² that about 40 per cent of all women with disseminated breast cancer can be found to have significant hypercalcemia at some phase of their disease. This figure is astonishing when you consider the body's numerous, highly efficient homeostatic mechanisms to keep the serum calcium level constant. Nature truly abhors hypercalcemia. Slight rises of the serum calcium level turn off parathyroid peptide secretion, stimulate the secretion of thyrocalcitonin and perhaps calcitonin, and the excess calcium is buffered in part by binding to serum proteins and, to a larger degree, taken up by bone.

This homeostatic point is brought out in Table 2, which shows the very narrow range of normal serum calcium one finds with modern, accurate methods. You will also note that women with disseminated breast cancer have slightly higher serum calcium and phosphate levels. Margottini,¹³ in Rome, has found similar values in women undergoing radical mastectomy and presumably free of metastasis. These slight but significant rises in serum calcium and phosphate suggested the possibility that breast cancer might lyse bone at a distance by some humoral mechanism.

That the hypothetical humor of breast cancer is not parathyroid peptide is strongly indicated by the fact that the serum phosphate and tubular reabsorption of phosphate are perfectly normal in women with the disease. In our laboratory, and using the identical techniques, patients with hyperparathyroidism uniformly have subnormal TRP's.

Furthermore, as Dent⁷ and Laird Myers¹⁴ showed, the hypercalcemia of breast cancer frequently responds to cortisone, while that of hyperparathyroidism rarely does. These considerations strongly indicated to us that the osteolytic humor in breast cancer is not parathyroid hormone.

Direct evidence that breast cancer does indeed contain an osteolytic factor was obtained by Dr.

Bernard Gardner, then a Research Fellow in our group and now Assistant Professor of Surgery at Downstate Medical Center in Brooklyn. He used the same technique Barnicot had previously devised to resolve the controversy of whether parathyroid hormone acts directly on bone. Barnicot implanted the parathyroid gland against the calvarium of rats and showed that it lysed the adjacent bone. Gardner⁸ similarly implanted bits of human breast cancer and found that the bone was lysed, contained great holes and fibrous replacement. Normal human breast tissue had no such lytic action. Lung cancers were also osteolytic and so was vitamin D. Now, Plimpton and Gellhorn¹⁵ had suggested, among other possibilities, that vitamin D might be the osteolytic factor in some malignancies. This seemed a real possibility and might explain the normal serum phosphate, the normal TRP and especially the response of the hypercalcemia of breast cancer to cortisone. So I took a sabbatical leave and assayed vitamin D in breast cancer in Dr. Schachter's laboratory in New York.

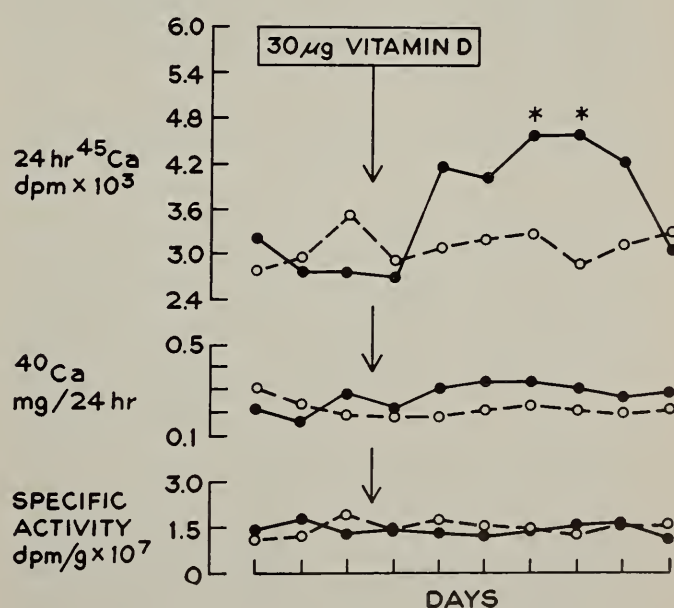


Chart 1.—Effect of Vitamin D on urinary calcium excretion of female rats with parathyroidectomy (solid line) and intact female rats with sham operation (broken line). *dpm=disintegration per minute; g=gram.

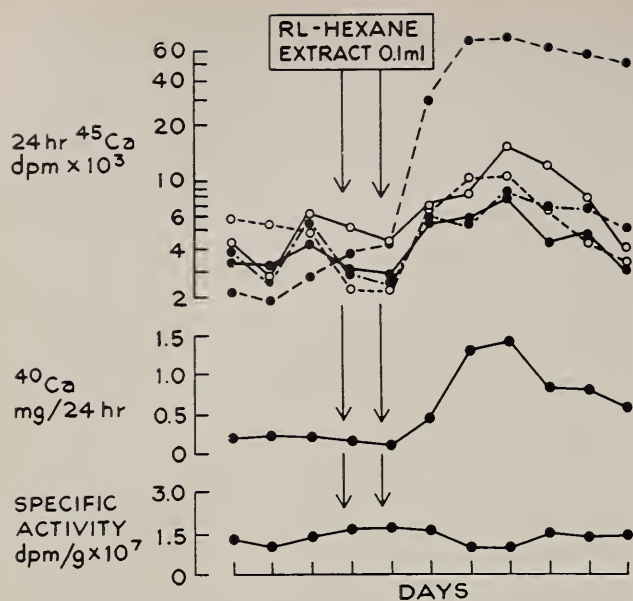


Chart 2.—Osteolytic activity found in hexane fraction indicating that osteolytic agent is a lipid. RL=from patient R.L.; dpm=disintegration per minute; g=gram.

We found that breast cancers do indeed contain small amounts of vitamin D, but normal breast contains much more.¹¹ Since normal breast does not lyse bone, it seemed unlikely that vitamin D was the malefactor in human breast cancer.

It therefore became necessary to develop an assay for osteolytic activity. After several false starts, we finally settled on the urinary radiocalcium excretion of the parathyroidectomized female rat whose skeleton has been labeled with ⁴⁵Ca. The animals are fed a near-zero diet so that the very small constant amounts of calcium, both stable and radioactive, in their urine come exclusively from bone.

The animals must have parathyroidectomy for this assay since the presence of the parathyroid gland prevents the calciuresis caused by well-known osteolytic agents such as vitamin D (Chart 1). We believe this phenomenon confirms Copp's idea that the parathyroid gland contains an anti-osteolytic factor, which he has named calcitonin. In the absence of the parathyroid, there is a brisk outpouring of radiocalcium and stable calcium. The specific activity remains that of bone, indicating that it does indeed come from bone.

We then made extracts from 12 breast cancers by the technique used for extraction of bovine parathyroid hormone. The peptide fraction, which would have contained parathyroid activity if any were present, was negative both for osteolytic activity and, by radioimmunoassay kindly performed by Drs. Berson and Yalow, for parathyroid pep-

tide. This result was not exactly unexpected—although gratifying—and we had saved the acetone-soluble fraction.

This was extremely potent for osteolytic activity and caused a very pronounced excretion of radio-calcium and stable calcium. Chart 2 shows that the osteolytic activity is in the hexane fraction, indicating that the osteolytic agent is a lipid. When the hexane fraction was placed on thin layer chromatography it separated into four distinct bands (Figure 1). Bands 1, 3 and 4 contain no osteolytic activity but Band 2 does. We have identified Band 2 in 11 of 12 breast cancers removed at mastectomy. Extracts from the same 11 tumors showed osteolytic activity.⁹

Neither Band 2 nor osteolytic activity could be found in extracts of four non-cancerous breasts. This figure also shows that Band 2 is in a different position from vitamin D. It has the bluish color of 7-dehydrocholesterol rather than the reddish color of cholesterol, but it moves slightly farther on thin layer chromatography. From its Liebermann-Burchard reaction, retention time on gas-liquid chromatography and ultra-violet and infrared spectra, this sterol has been identified as a member of the 7-dehydrocholesterol group. You will recall that 7-dehydrocholesterol is pro-vitamin D₃. Exact identification of the sterol is in progress.* So far, the osteolytic sterol has been shown only in breast cancers. We hope to look for it soon in other conditions.

I should like to end on a clinical note. Perhaps it seems unimportant to diagnose and treat hyper-

*The osteolytic sterols in human breast cancer have subsequently been identified as 7-dehydrositosterol acetate, stigmasteryl acetate and stigmasterol. (Gordan, G. S., Fitzpatrick, M. E., and Lubich, W. P.: Trans. Assoc. Amer. Phys., 1967. In press.)

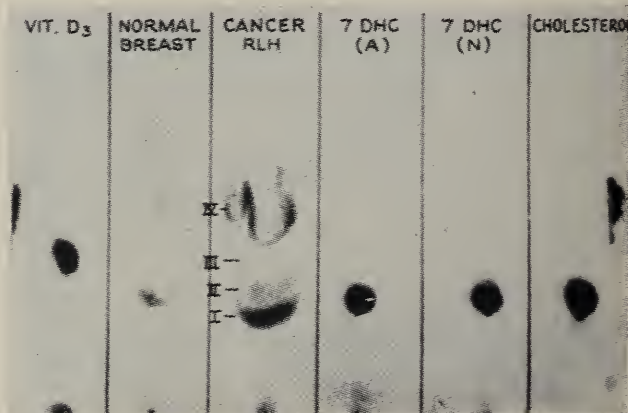


Figure 1.—Thin-layer chromatogram of hexane extracts derived from normal and neoplastic human breast with reference to sterols. (RLH=Hexane extract from patient RL; DHC=Dehydrocholesterol; (A)=Ayerst Laboratories; (N)=Nutritional Biochemicals Corp.).

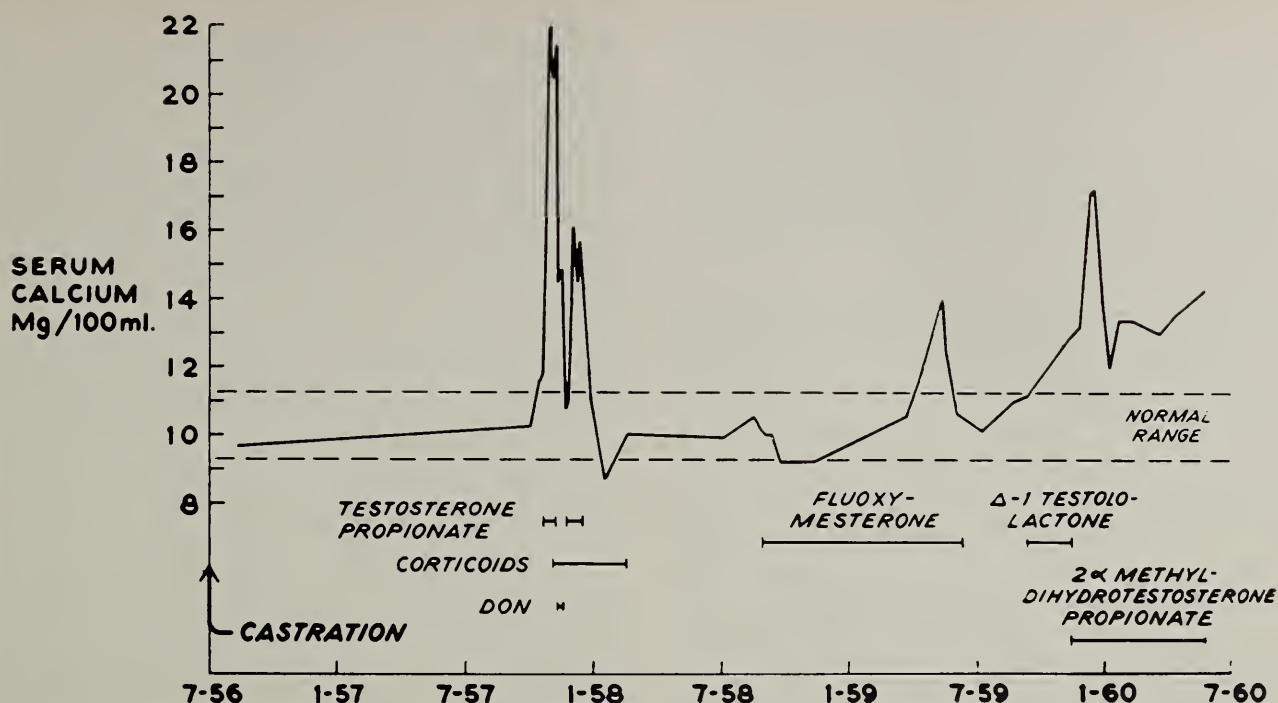


Chart 3.—Response to antimetabolite DON (diazooxonorleucine) by patient with hypercalcemia due to osteolytic metastasis of breast cancer.

calcemia in a patient doomed to die of disseminated cancer. I do not subscribe to this point of view and would like to show the case of a woman who came into this hospital in September 1957 in coma with serum calcium of 22 mg per 100 ml (Chart 3). She was riddled with osteolytic metastasis of breast cancer which had not responded to mastectomy, castration or testosterone propionate. The hypercalcemia did not respond to the usual measures (hydration or corticoids) but did respond to an antimetabolite—in this case diazooxonorleucine (DON). Hydration, in our experience, is by itself effective treatment in more than half of cases. Corticoids raise this figure to 81 per cent. The chelator versene had a vogue but has been abandoned because of its renal toxicity. The divalent anions sulfate and phosphate are effective in all kinds of hypercalcemia, and phosphate was used with good chemical results in the case presented today. Phosphate has been used successfully since the reports of Bulger and coworkers⁵ in 1930 and of Albright and coworkers² in 1932. Just now it is all the vogue in the treatment of hypercalcemia. It is certainly effective in acute episodes, but probably deposits calcium phosphate in unwanted sites so should not be used chronically. For this reason I much prefer intravenously administered sulfate.^{6,17} In the case I have just discussed, thanks to the heroic efforts of the house staff, the patient survived. She lived four and a half years, for the

most part comfortably. She enjoyed camping and hunting and occasionally brought us gifts of venison, not always, I noted, during hunting season. The point I wish to make is that vigorous treatment of hypercalcemia gave this woman over four years of comfortable life. The moral, I think, is that the tumor, though widespread, may be indolent, so it is important to recognize and treat hypercalcemia. In the absence of metastasis, hypercalcemia may be the initial and only clue to the diagnosis of curable cancer. But even when the tumor is incurable the diagnosis and treatment of hypercalcemia can add years to life and—more important—life to years.

DR. SMITH: I am intrigued that Dr. Gordan passed so quickly over the possibility that this might be a parathyroid peptide based entirely on the serum phosphate. Did Dr. Tashjian in his studies find a close correlation in phosphate level and the identification of the peptide?

DR. GORDAN: Actually neither Dr. Tashjian in his published papers nor Dr. Melick who has done similar work with the Berson-Yalow radioimmunoassay has published the effect of the correlation of the serum phosphate, but through personal communication I have learned that these people had the typical hyperparathyroid syndrome with hypercalcemia and a low serum phosphate

level.* This brings up the one point that the patient we are discussing today had a serum creatinine of 1.8 mg per 100 ml and one might say that perhaps it was elevated by renal insufficiency. Of course, in a man the serum creatinine is usually about 4 mg per 100 ml before the serum phosphate starts to rise, and I would pass over it on that ground alone.

DR. SMITH: In this particular patient do you feel the osteolytic metastatic lesions were the most likely cause of hypercalcemia?

DR. GORDAN: I had hoped that Dr. Bailey would say a little more about this. He did find a few osteolytic lesions of metastasis. Of course, one does not usually make serial sections of the entire skeleton, so we cannot say just how many there were, but they seem to be few in number. I am really quite partial to this humoral mechanism and I hope that we will soon be in a position to answer this question. Until we have the complete identification and a chemical method of measuring the compound in blood, we cannot really say whether this sterol is present in cancer, whether it signals recurrence, or whether it is indeed responsible for hypercalcemia.

DR. SMITH: Many of us are intrigued by the fact that malignant tumors seem to produce true hormones under certain circumstances. This is perhaps not so surprising as it seems at first glance. Actually the real mystery, and one of the major problems in biology at the present time, is not why some cells are able to form specialized compounds such as hormones but why they do not form them all the time. As we know, all evidence suggests that each cell in the body contains the genetic information necessary to make all of the proteins or enzymes that any other cell can make. Thus, the real mystery lies in the mechanism by which the expression of some of these genes is blocked in the normal differentiation of the cell. Perhaps in malignant disease there is "uncovering" of the genetic code as part of the process of anaplastic growth. I find it very intriguing to speculate that the genetic code may be rather broadly uncovered and this cell may be making other proteins in addition to hormones—for example, serum albumin or gammaglobin or chymotrypsin. However, it is only the hormonally active proteins which become clinically evident in such minute

amounts. There is no means of identifying whether this tumor is also producing micro amounts of serum albumin. It might very well be doing so. It is interesting that one of the few endocrine syndromes which has not been found with extra-endocrine malignant lesions is that of growth hormone excess. Perhaps this is because growth hormone is required in milligram rather than microgram amounts.

DR. GORDAN: This is the current concept as proposed by Gellhorn, by Lipsett, by Tashjian and most extensively by Ivan Bennett. It holds that the loss of the repressor mechanism makes an anaplastic carcinoma cell totipotent, as cells presumably were once, so that they all make everything. I do not like this theory. If it were true, one would expect all of these cells to be making all of these things and probably the same sort of syndromes would occur. If one looks at the kinds of syndromes that occur with malignant disease, he will note that there is a certain kind of specificity for the hormone produced. For example, breast cancer *never* makes parathyroid peptide or ACTH.

Dr. Bower and I have come up with a different thesis. We were struck by the fact that tumors that make the material that acts like thyrotrophin are all making chorionic gonadotrophin to start with, and we suggested the possibility that when they make these proteins or peptides, the sequence is already present, so it is only necessary to add or knock off an amino acid here or there and instead of making chorionic gonadotrophin, one would end up with something like thyrotrophin. In fact, there is some support for this because Werner in New York recently showed that you can make a whole group of amino acid and peptide derivatives that have thyrotrophic activity. The specificity makes me believe that it is not just the loss of the depressor mechanism.

In addition, if the mechanism were loss of a depressor, the humor formed would be the authentic hormone. Odell recently showed that the thyrotrophic substance formed by trophoblastic malignant disease is immunologically distinct from authentic thyrotrophin. Clearly, therefore, the depressor mechanism does not hold in this particular case. (Odell, W. D., Wilber, J. F., and Paul, W. E., *J. Clin. Endocrinol.*, 25:1179, 1965.)

DR. SMITH: You are requiring totipotent messenger RNA rather than totipotent cells then? Neither one of us can disprove the other—that is the advantage of this kind of exchange.

*Subsequently published by Sherwood, L. M., O'Riordan, J. L. H., Aurbach, G. D., and Potts, J. T., Jr., *J. Clin. Endocrinol.*, 27:140, 1967.

DR. EISENBERG^{*5}: I would like to return to a clinical note as we close this discussion. In most cases hypercalcemia does respond to low calcium intake, hydration and, in some instances, corticoids. Patients with hypercalcemia severe enough to require other acute therapy often have other severe complications and the mortality rate among them is high. There are drawbacks to all intravenous therapies for hypercalcemia. Ethylenediamine tetracetic acid (EDTA) is nephrotoxic, sulfate requires good renal function, which often is not present, and phosphate may cause calcium phosphate precipitation in vital areas such as lung and kidney. I believe that intravenous sodium phosphate will prove not to be good therapy for acute hypercalcemia. The usefulness of oral phosphate therapy for less severe cases is another matter. I personally would favor the use of hemodialysis for control of severe hypercalcemia in acute episodes. Since all forms of therapy are temporary, one must develop a plan for long term management of the disease process. In other words, all of these therapies only buy us a little time.

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EDITORIAL

New President-Elect Of the AMA

AS A FORWARD LOOKING component of the American Medical Association, the California Medical Association is highly pleased with the unanimous election of one of its outstanding members as president-elect of the national organization.

Certainly for our profession, and for many friends outside it, a warming element of the election of Dr. Dwight L. Wilbur to that position was that it marked the first time in AMA's history that a son of a former president has been named for elevation to the presidency. The new president-elect is the son of the late Ray Lyman Wilbur, M.D., who was president in 1923-24 and who also will be remembered as Secretary of the Interior in the cabinet of President Herbert Hoover and as president and later chancellor of Stanford University.

In California it is doubly gratifying to our sense of tradition and fitness that Dr. Wilbur will be installed as president of the AMA when it meets next year in San Francisco, where he practices medicine.

My own pleasure in the election was the greater because, as spokesman for our state association, mine was the privilege of nominating the successful



DWIGHT L. WILBUR, M.D.

President-elect of the
American Medical Association

candidate. Now I would like to extend a feeling of participation in the event, both for myself and all the members of the California Medical Association, by giving a somewhat fuller description of the next president of the AMA than was appropriate in a nominating speech.

Dr. Dwight L. Wilbur, who is known for his service as a practicing physician, teacher, editor and public servant, was born 18 September 1903

in Harrow-on-the-Hill, England, while his father was doing postgraduate studies in Europe.

In 1923 Dr. Wilbur received his A.B. degree in zoology, with distinction, from Stanford University, and there was elected to the scholastic honor society, Phi Beta Kappa. Three years later he was awarded his medical degree, with honors, at the University of Pennsylvania and was inducted into Alpha Omega Alpha. In 1933 Dr. Wilbur received an M.S. degree in medicine from the University of Minnesota, where he became a member of Sigma Xi.

From 1926 to 1928 he was resident physician in the hospital of the University of Pennsylvania and during the following two years a fellow in medicine at the Mayo Foundation. From 1931 to 1937 Dr. Wilbur was a consulting physician at the Mayo Clinic.

For the past 30 years he has been on the clinical faculty at the Stanford University School of Medicine and since 1949 has been clinical professor of medicine.

An internist and gastroenterologist, Dr. Wilbur has been both a group and solo private practitioner for 36 years. For the past 20 years he has practiced in partnership with four internists in San Francisco.

During World War II he served for four years as a Lt. Commander and Commander in the Medical Corps of the U.S. Navy stationed at the U.S. Naval Hospital in Oakland.

Following his discharge he has continued to assist the government in various civilian capacities including: Membership on the Civilian Health and Medical Advisory Council to the Secretary of Defense; a member of the medical task force of the Second Commission on Organization of the Executive Branch of Government (Hoover Commission); as a member of the National Advisory Commission on Health Manpower.

Since 1946 Dr. Wilbur has been chief of Medical Service at French Hospital in San Francisco. He is also a member of the staff at Presbyterian Medical Center, Children's and St. Francis Memorial hospitals in that city. Dr. Wilbur is also a consulting physician to the Southern Pacific Hospital in San Francisco, the U.S. Naval Hospital in Oakland, Letterman General Hospital in San

Francisco and the Veterans Administration Hospital in Martinez.

During the past 21 years he has served as editor of CALIFORNIA MEDICINE, official journal of the California Medical Association. From 1943 to 1964 he was associate editor and later chairman of the editorial board of *Gastroenterology*, official publication of the American Gastroenterological Association. Dr. Wilbur is also the author of numerous scientific articles on the kidney, gastrointestinal tract, and nutrition.

He was first elected a delegate from California to the AMA House of Delegates in 1942. During the intervening years Dr. Wilbur served a total of 17 years as a delegate. He has been a member of the council of his state medical association since 1946.

He was elected to AMA's Council on Medical Education in 1961, and before that had served for a number of years as secretary, vice chairman, and chairman of AMA's Scientific Section on Experimental Medicine and Therapeutics.

In 1963 the AMA House of Delegates elected Dr. Wilbur to the Board of Trustees of the Association. He was re-elected for a second three-year term in 1966.

Dr. Wilbur is chairman of the Board Committee on Health Manpower, was a member of the Study Committee on Planning and Development, and a member of the Advisory Committee to the Department of Health, Education, and Welfare.

He is also a commissioner and chairman of the AMA commissioners to the Joint Commission on Accreditation of Hospitals.

Dr. Wilbur is a past president of the American Gastroenterological Association and of the American College of Physicians. His stature in scientific medicine and as an internist is indicated by his membership in the American Society for Clinical Investigation and the Association of American Physicians, by the award to him of the Julius Friedenwald Medal of the American Gastroenterological Association for distinguished achievement in the field and by his selection for mastership in the American College of Physicians. He has also served as a member of the Subcommittee on Food and Nutrition of the National Research Council and on a committee of the National Institute of

Arthritis Metabolic Diseases. He is a diplomate of the American Board of Internal Medicine.

During the years, Dr. Wilbur has maintained his affiliation with the Mayo Foundation. He has served as a member of the Board of Trustees of the Mayo Foundation since 1951 and is now president of the Alumni Association of the Mayo Graduate School of Medicine.

Dr. Wilbur is married to the former Ruth Esther Jordan and they are the parents of three sons, two of whom are physicians.

From this dossier we may have some measure of the personage who less than a year from now will become the leader of the world's greatest medical association. But to know him better, we must look at him more as a person than a personage.

We in California know him for his hard work—hard successful work—for his county medical association and his state association, and for highly innovative participation in all aspects of medical civics.

Up to now I have spoken of Dr. Wilbur's abilities, his accomplishments, his capacity for work, his stature in our profession and in our greatest medical organization. But this account must show also that he can play, as well as work. When the season rolls around and the duck blinds beckon, he can be found with the others, waiting his chance. He knows also the fisherman's peculiar joy of wading through poison oak and cold water in the Klamath River country to hook a steelhead. Dr. Wilbur can also loaf prodigiously. I am told that this man, known to many of his fellow physicians as well-groomed and industrious, can in his days of leisure at his farm a few miles from San Francisco, look and apparently feel like the veriest one-gallus loafer who ever whittled away an afternoon at a cross-roads store.

Finally, any accurate sum of the new president-elect must include this: He inspires loyalty and respect in those who work with him.

JOHN G. MORRISON, *President*
California Medical Association

A Memorial for Dr. Charles E. Smith

THE CORPOREAL LIFE OF Dr. Charles E. Smith, dean of the University of California School of Public Health, Berkeley, has ended but the lamps he lit with his teaching, his scientific searches, his counsel and his friendships burn on.

Dr. Smith, known the world over as an authority on coccidioidomycosis, was widely honored not only for his researches in this disease but for outstanding ability as a teacher and administrator in his chosen field of medicine. He was a sound, approachable expert in Public Health whose stature was well measured at the time of his death by Dr. Lester Breslow, director of California's State Department of Public Health: "Dr. Smith was our first thought in any crisis."

Dr. Smith was president of the State Board of Public Health for 20 years. He was a holder of the John G. Sippy Award of the Western Branch of the American Public Health Association and of the APHA's Bronfman Prize for international achievement in public health.

CALIFORNIA MEDICINE had particular reason to value him highly, for he worked hard, long and amiably as a member of this journal's Editorial Board for 20 years.

Of all the honors that came to him, those that probably pleased him most were the informal ones that come to a teacher whose students keep in touch with him long years after graduation. He was their friend and was delighted more by their achievements than by any of his own. He knew special gratification in this long extension of the relationship of teacher to student: "They've taught me more" he once said, "than I ever taught them."

For that reason the form of a memorial that his friends have selected to honor the memory of this extraordinary man is particularly appropriate—The Charles E. Smith Student Loan Fund to help students finance their education in Public Health.*

*Contributions may be made by check drawn to the Regents of the University of California, with the additional note, "Charles E. Smith Student Loan Fund." Checks should be addressed to the University of California School of Public Health, Earl Warren Hall, Berkeley, California 94720.

California Medical Association



NOTICES AND REPORTS

Wilbur Named AMA President-Elect; Davis to Board of Trustees

Dr. Dwight L. Wilbur was unanimously elected president-elect of the American Medical Association at the 116th annual convention in Atlantic City (see editorial, page 62), and Dr. Milford O. Rouse was installed as president.

The new president-elect had been a member of the AMA's Board of Trustees since 1963. He has been editor of *CALIFORNIA MEDICINE*, the official journal of the California Medical Association, for 21 years, and by virtue of that office has sat as a member of the CMA Council for the same period.

When he is inducted as AMA president a year from now, Dr. Wilbur will be the first president whose father also held that office. Dr. Ray Lyman Wilbur was president in 1924.

Dr. Burt L. Davis of Palo Alto was elected to complete Dr. Wilbur's unexpired term on the AMA Board of Trustees.

Dr. Davis is on the faculty of Stanford University School of Medicine as a member of the Department of Anatomy, and is a member of Sigma Xi and Alpha Kappa Kappa. He has been a member of the California Medical Association House of Delegates for 23 years, and he served for six years

on the CMA Council, three years as vice-chairman. For six years he was a member of the CMA Finance Committee, three years as chairman. He was also a member of the CMA Cancer Commission for six years, two as chairman. He was one of the founders of the CMA Bureau of Research and Planning, and has continued in various capacities with its development. Currently he is a member of the Committee on the Role of Medicine in Society.

For eight years a member of the board of trustees of the California Blue Shield Plan, he is now serving his second year as a member of the board of directors of the National Association of Blue Shield Plans representing District XI (the United States and Canada west of the Rocky Mountains, and Hawaii).

The new AMA trustee was alternate delegate to the AMA from California from 1952 to 1960, during which time he was active in securing participation for all alternates in AMA activities. He has been a delegate since 1960. He was elected vice-

| | |
|--------------------------------------------------------------------|------------------------------|
| JOHN G. MORRISON, M.D. | President |
| MALCOLM C. TODD, M.D. | President-Elect |
| WILLIAM F. QUINN, M.D. | Speaker |
| JOSEPH F. BOYLE, M.D. | Vice-Speaker |
| ALBERT G. MILLER, M.D. | Chairman of the Council |
| HAROLD KAY, M.D. | Vice-Chairman of the Council |
| HELEN B. WEYRAUCH, M.D. | Secretary |
| DWIGHT L. WILBUR, M.D. | Editor |
| HOWARD HASSARD | Executive Director |
| General Office, 693 Sutter St., San Francisco 94102 • 415 776-9400 | |
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| 1515 N. Vermont Ave., Los Angeles 90027 • 213 663-8071 | |
| RICHARD W. LEMOS Sacramento Office | |
| 1127 11th St., Sacramento 95814 • 916 444-7496 | |

chairman of the delegation in 1961 and became chairman last year.

Early in the development of the Academy of General Practice, Dr. Davis became speaker of the California Congress of Delegates, and he was President of the California Academy of General Practice in 1961-62.

In community affairs, he served for six years as a councilman for the City of Palo Alto, was a director of the California Division of the American

Cancer Society for eight years, and has been chief of staff of the Palo Alto-Stanford Hospital.

With Dr. Davis' election to the Board of Trustees, the CMA delegation to the AMA House of Delegates elected Dr. Eugene F. Hoffman Sr. of Los Angeles, long a member of the delegation and a former CMA Councilor, to the chairmanship formerly held by Dr. Davis. Dr. Samuel R. Sherman, a past-president of CMA and a former chairman of the Council, was elected vice-chairman.



ACTIONS OF THE HOUSE OF DELEGATES

Los Angeles, April 14 to 19, 1967

NOTE: *The following report of the transactions of the House of Delegates of the California Medical Association is selected and abridged. A complete transcript of all proceedings is on file in the Association office in San Francisco and available for the inspection of all members.*

REFERENCE COMMITTEES

COMMITTEES APPOINTED by Speaker William F. Quinn at the first meeting of the House of Delegates Saturday evening, April 15, were as follows:

Committee on Credentials: A. J. Murrieta, Jr., Los Angeles, chairman; A through L component societies: Thomas Elmendorf, Willows; George S. Buehler, Whittier; George C. Andersen, Hermosa Beach; Paul D. Yates, Hermosa Beach, and Bernard Axelrod, Los Angeles.

M through Z component societies: Jack W. Baker, Temple City; S. A. Skillicorn, San Jose; Tom M. Fullenlove, San Francisco; Donald J. Barry, Arcadia, and Gordon Bowen, Lynwood.

Reference Committee 1: (This committee reviews the reports of the officers, the Council, the commissions and standing and special committees.) Oscar W. Hills, San Mateo, chairman; John A. Bullis, Los Angeles; Gerald Ingle, Corning; Harold Messenger, San Diego, and Harvey E. Starr, Los Angeles.

Reference Committee 2: (This committee on finance reviews the reports of the secretary, executive secretary and studies and makes recommendations to the House of Delegates on the budget submitted by the Council and on the amount of dues for the ensuing year.) Norman C. Fox, San Bruno, chairman; Ralph M. Milliken, Los Angeles; George Herzog, Jr., San Francisco; Chester Tancredi, San Diego, and A. E. Berman, Sacramento.

Reference Committee 3: (This committee con-

siders new and miscellaneous business.) Robert L. Hippen, San Diego, chairman; Robert T. Hood, Jr., Van Nuys; Harold Miles, Santa Barbara; E. Kash Rose, Napa, and Fred Ackerman, Pleasant Hill.

Reference Committee 3A: (To consider business of Committee 3 when the volume becomes too great for one committee to handle.) H. Dean Hoskins, Oakland, chairman; Leonard M. Asher, Beverly Hills; M. M. Haskell, Long Beach; Vincent Carroll, Laguna Beach, and Glenn A. Pope, Sacramento.

Reference Committee 3B: (This committee also is a supplement to 3 and 3A.) J. B. Price, Santa Ana, chairman; Gerald Besson, Sunnyvale; Chester E. Herrod, San Francisco; Charles B. Hudson, Oakland, and Homer C. Pheasant, Los Angeles.

Reference Committee 4: (This committee considers amendments to the Constitution and By-laws.) Ralph M. King, La Mesa, chairman; Robert L. Day, Bakersfield; Mason Hohl, Beverly Hills; Ralph D. Beasom, Los Angeles, and Marvin J. Shapiro, Encino.

California Blue Shield (CPS) Reference Committee: (This committee considers new and miscellaneous business pertaining to California Blue Shield (California Physicians' Service).) Robert C. Combs, San Francisco, chairman; Roger W. Barnes, Los Angeles; Herbert Holden, San Leandro; Herman H. Stone, Riverside, and John E. Vaughan, Bakersfield.

PRESENTATION OF FIFTY-YEAR AWARDS

Pins commemorative of 50 years of membership in the California Medical Association were presented to the following physicians: Alameda-Contra Costa: Milton H. Shutes; Kern: A. Russell Moodie; Los Angeles: Benjamin Frees, Carl W. Rand, Paul B. Roen; San Diego: Martha Welpton; San Francisco: Lloyd B. Crow, Edward Harrington, Henry Stephenson.

RECOGNITION AND AWARDS

James C. MacLaggan was presented a plaque for his two years of dedicated service to the CMA as President and President-Elect. John G. Morrison was presented the President's gavel.

Plaques for outstanding contributions were presented to Mr. Rueben M. Dalbec as outgoing chairman of the Medical Executives' Conference and to Mr. Everett Bannister for his service to the Orange County Medical Association.

A standing ovation was accorded Carl E. Anderson, outgoing Chairman of the Council, for his dedicated service. Dr. Anderson was presented with a silver gavel, a clock, a fishing rod, and a plaque.

ELECTIONS

OFFICERS (One Year Terms)

John G. Morrison, San Leandro, was installed as President. Malcolm C. Todd, Long Beach, was elected President-Elect. William F. Quinn, Los Angeles, was re-elected Speaker of the House of Delegates. Joseph F. Boyle, Los Angeles, was elected Vice Speaker of the House of Delegates.

COUNCIL (Three Year Terms)

First District—Stanley A. Moore, San Diego; Third District—Henry V. Eastman, Tustin; Fourth District-Office No. 3—Homer C. Pheasant, Los Angeles; Fourth District-Office No. 6—Marvin J. Shapiro, Encino; Fourth District-Office No. 9—Joseph F. Boyle, Los Angeles. Fifth District—Joseph F. Maguire, Ventura; Seventh District-Office No. 1—Richard S. Wilbur, Palo Alto;

Eighth District-Office No. 2—Roberta Fenlon, San Francisco; Ninth District-Office No. 2—William F. Kaiser, Berkeley; Tenth District—E. Kash Rose, Napa; Twelfth District—Forest J. Grunigen, Los Angeles.

AMA DELEGATION (Two Year Terms)

Starting January 1, 1967

Delegate, Carl E. Anderson.

Alternate, Jean F. Crum.

Starting January 1, 1968

DELEGATES

Francis E. West, San Diego; Samuel R. Sherman, San Francisco; Albert G. Miller, San Mateo; John M. Rumsey, San Diego; Eugene F. Hoffman, Sr., Los Angeles; Warren L. Bostick, Los Angeles; Vincent P. Carroll, Laguna Beach; Ralph C. Teall, Sacramento; James C. Doyle, Santa Monica; Wilbur G. Rogers, Glendale; Charles B. Hudson, Oakland.

ALTERNATES

Laurance A. Mosier, Garden Grove (alternate to Francis E. West). George K. Herzog, Jr., San Francisco (alternate to Samuel R. Sherman). A. B. Sirbu, San Francisco (alternate to Albert G. Miller). Robert T. Hood, Jr., Van Nuys (alternate to John Rumsey). Joseph F. Boyle, Los Angeles (alternate to Eugene F. Hoffman Sr.). Walter H. Brignoli, St. Helena (alternate to Warren L. Bostick). William F. Kaiser, Berkeley (alternate to Vincent P. Carroll). Robb Smith, Orange Cove (alternate to Ralph C. Teall). Herman H. Stone, Riverside (alternate to James C. Doyle). Ben D. A. Miano, San Bernardino (alternate to Wilbur G. Rogers). Robert L. Watson, Jr., Los Angeles (alternate to Charles B. Hudson).

BOARD OF TRUSTEES OF THE CALIFORNIA PHYSICIANS' SERVICE (Three Year Terms)

Richard S. Wilbur, M.D., Palo Alto; Harold Messenger, M.D., San Diego; Mr. Frank R. McDougall, San Diego; Mr. C. E. Pigg, Van Nuys; Mr. Clinton Fair, San Francisco.

REFERENCE COMMITTEE RECOMMENDATIONS

Reference Committees are encouraged to comment on any activity of the California Medical Association that comes to their attention. If these observations or recommendations are not directed toward a specific resolution, constitution or bylaw amendment, they are recorded in this section. Referrals were made by the Council at its meeting May 27, 1967.

REFERENCE COMMITTEE NO. 1

REPORTS

It is recommended that:

1. The artful, informative and readable expression of CMA Physician activity, *Strengthening Health Care for Californians*, should receive the widest possible professional and public exposure.

2. Consideration be given to the preparation and publication of a similar report of CMA achievements annually.

Referred to: Council and Commission on Communications.

3. The Council and Editor of CALIFORNIA MEDICINE give consideration to the inclusion in the CMA Journal of a distinctive scientific information page highlighting recent reports of scientific interest.

Referred to: Council and Editor.

4. The appointment of Reference Committee No. 1 should be made as soon as possible after each Annual Session.

5. This committee should meet as often as necessary during the year following their appoint-

ment and preceding the Annual Session at which they will be expected to report.

6. The committee meetings should be held at the CMA headquarters in San Francisco, where current commission and committee information and background materials are readily available.

Referred to: Speaker of the House of Delegates.

REFERENCE COMMITTEE NO. 2

FINANCE

The committee recommends that a copy of the detailed Budget be mailed to each Component Medical Society prior to the Annual Meeting. Additional audiovisual aides and a more detailed summary should be provided at the hearing.

The committee urges continued review of the role this Association should play in financing medical libraries and the California Medical Library Association.

Referred to: Finance Committee.

REFERENCE COMMITTEES NOS. 3, 3A and 3B

NEW BUSINESS

Recommendations are a part of the report on the resolutions.

REFERENCE COMMITTEE NO. 4

CONSTITUTION AND BYLAWS

Recommendations are a part of the report on the constitutional amendment or bylaw change.

REFERENCE COMMITTEE ON THE CALIFORNIA BLUE SHIELD (CPS)

Recommendations are a part of the report on the resolutions.

ACTION ON RESOLUTIONS

ONE HUNDRED AND EIGHT RESOLUTIONS came before the 1967 House of Delegates. Each was numbered and assigned to a Reference Committee for consideration and recommendation.

Reference Committees have the option of recommending a resolution for adoption or rejection, for adoption as amended or substituted, or for no action.

Resolutions shown here are in the form in which the House of Delegates approved them for adoption or for referral to the Council or to specified commissions or committees. Where a resolution was not adopted, that report is made here but the language of the resolution is not shown. Copies are available in the CMA office on request.

Each resolution is shown by number and subject and the name and status of each author is recorded.

The action reported at the foot of each resolution was taken by the House of Delegates, April 18 and 19, 1967. The referrals were made by the Council at its meeting, May 27, 1967.

1 1 1

WELFARE PRESCRIPTION FORMS

Resolution No. 1-67

Committee 3A

Introduced by: James W. Goettle, M.D.

Representing: Tulare County Delegation

WHEREAS, physicians in California are scarce and overworked; and

WHEREAS, added paper work and multiplication of forms is in increasing problem requiring more and more time from the physician and his staff, and since much of this paper work is instigated by government agencies; now, therefore, be it

Resolved: That the California Medical Association recommend that its members use their own standard prescription forms for all patients, rather than special forms (such as MC-165 of the Department of Social Welfare).

ACTION: *Referred to Council.*

Referred to: Commission on Public Agencies.

1 1 1

RVS IDENTITIES FOR STAFF SUPERVISION OF PUBLIC HOSPITAL TRAINEES

Resolution No. 2-67

Committee 3A

Introduced by: Leon P. Fox, M.D.

Representing: Santa Clara County Medical Society

WHEREAS, Title 18 and 19 of Public Law 89-97

and the implementing state laws have jeopardized the intern-resident training programs in the many public hospitals in California; and

WHEREAS, these public hospitals are an essential source of practicing and teaching physicians in a constantly growing California and National population with an increasing physician shortage; and

WHEREAS, certain revisions of the law as well as additional implementing procedures can improve the present dilemma and perpetuate this traditional fountainhead of graduate medical education; and

WHEREAS, California public hospitals have already contracted with their medical staffs to divert professional fees obtained for services to non-private patients into a fund to be used for financial support of the training program; and

WHEREAS, presently there is little if any remuneration to the medical staff members for their participation in the training program and minimal support from local governments for same; and

WHEREAS, the AMA House of Delegates has approved of the principle of charging for these professional services and utilizing such fees as herein suggested (Report R, Board of Trustees, November 1966 at Las Vegas); and

WHEREAS, in California the Relative Value Schedules for usual and reasonable fees have been referred to by the present insurance carriers for Medi-Cal and Medicare; now, therefore, be it

Resolved: That the California Medical Association direct its Committee on Fees to establish and define a supervisory teaching experience relative value entity for all listed procedures in accordance with its representation of responsibility and time consumption of the supervising physician; and be it further

Resolved: That the appropriate committees negotiate with the pertinent insurance carriers endeavoring to establish the philosophy and implementation of this resolution; and be it further

Resolved: That the California Delegation to the American Medical Association be directed to introduce a similar appropriate resolution before the House of Delegates of the AMA in June 1967.

ACTION: *Referred to Council.*

Referred to: AMA Delegation.

CERTIFICATION AND RECERTIFICATION

Resolution No. 3-67

Committee 3A

Introduced by: Merlin A. Hendrickson, M.D.

Representing: San Bernardino County Medical Society

WHEREAS, there has been confusion, harassment and abuses over the interpretation and implementation of the certification and recertification mechanism; and

WHEREAS, to ease tensions and promote better understanding; now, therefore, be it

Resolved: That the CMA Model Medical Staff By-laws include the statement, "The Medical Staff recognizes the physician's signature on the patient's chart, or following his orders therein, as certification of the medical necessity of the patient's admission and for his continued treatment in the hospital"; and be it further

Resolved: That this action and recommendation be widely disseminated to all interested parties.

ACTION: *Referred to Council.*

Referred to: Commission on Hospital Affairs.

‘ ‘ ‘

CERTIFICATION AND RECERTIFICATION

Resolution No. 4-67

Committee 3A

Introduced by: Merlin A. Hendrickson, M.D.

Representing: San Bernardino County Medical Society

ACTION: *No action was taken on this resolution.*

‘ ‘ ‘

DIRECT BILLING AND ASSIGNMENT MECHANISM

Resolution No. 5-67

Committee 3A

Introduced by: Merlin A. Hendrickson, M.D.

Representing: San Bernardino County Medical Society

ACTION: *No action was taken on this resolution.*

‘ ‘ ‘

DEPARTMENT OF REHABILITATION REPORT FEES

Resolution No. 6-67

Committee 3

Introduced by: Santa Clara Delegation

WHEREAS, the California State Department of Rehabilitation requires certain information for their clients which must be obtained from physicians (Form SSA-826); and

WHEREAS, this requires abstracting the medical record by the client's physician; and

WHEREAS, this record is frequently lengthy and complicated; and

WHEREAS, the Department of Rehabilitation does not have budgetary provision to remunerate the physician for this report; and

WHEREAS, physicians are remunerated by other

agencies of government for medical reports; and

WHEREAS, the failure of the Department of Rehabilitation to remunerate physicians for completing these forms is an inequity; now, therefore, be it

Resolved: That the California Medical Association's House of Delegates instruct the California Medical Association Council to investigate and urge that all federal and state departments provide funds for remuneration of physicians for necessary medical reports furnished to them.

ACTION: *Adopted as amended.*

Referred to: Commission on Medical Service.

‘ ‘ ‘

THE PASTEURIZATION OF MARKET MILK

Resolution No. 7-67

Committee 3B

Introduced by: Stanley A. Skillicorn, M.D.

Representing: Santa Clara County Medical Society

WHEREAS, milk and milk products are among the most perishable and potentially dangerous foods; and

WHEREAS, outbreaks of tuberculosis, brucellosis, scarlet fever, diphtheria, Q fever, salmonellosis, and other diseases have been traced to unpasteurized or raw milk; and

WHEREAS, raw milk has been proven a constant reservoir of Enterotoxigenic Staphylococcus of both human and animal origin which serves as a potential threat to public health; and

WHEREAS, pasteurization has proven the one safe, effective and efficient method of insuring safe milk; and

WHEREAS, there have been no proven deleterious effects upon the food value of milk due to the pasteurization process; and

WHEREAS, 3,380 gallons of unpasteurized milk are sold in California daily; and

WHEREAS, 39 states, and over 2,000 cities and counties in the United States prohibit the public sale of raw milk; now, therefore, be it

Resolved: That the California Medical Association recommends that all market milk sold for human consumption in the State of California be pasteurized; and be it further

Resolved: That the California Medical Association requests the State of California Department of Public Health, with the cooperation of the State Department of Agriculture, the dairy industry and other interested groups, to prepare legislation to prohibit the sale of raw milk for human consumption in California.

ACTION: *Adopted.*

Referred to: Legislative Committee.

PHYSICIANS' EMPLOYEES' HEALTH COVERAGE BY CPS-BLUE SHIELD

Resolution No. 8-67

California Blue Shield Committee

Introduced by: San Francisco Delegation

WHEREAS, many physicians are interested in having insurance coverage for their employees; and

WHEREAS, it would be possible for CPS to institute appropriate eligibility certification; now, therefore, be it

Resolved: That CPS offer physicians' employees health insurance, with proper safeguards for the plan's protection.

ACTION: *Adopted as amended.*

Referred to: CPS-Blue Shield Board of Trustees and Commission on Professional Welfare.

QUALITY CARE

Resolution No. 9-67

Committee 3

Introduced by: San Francisco Delegation

WHEREAS, there is increasing demand for on-going review of the quality of medical care as it is practiced outside of hospitals, similar to that in hospitals; and

WHEREAS, self-surveillance by the medical profession itself is recognized by physicians and others as preferable to review by non-physicians; now, therefore, be it

Resolved: That an appropriate Committee of the CMA investigate methods to study factors in the practice of medicine outside of hospitals, to evaluate indices of the quality of medical care, and to develop techniques to appraise the work of individual physicians through the proper committees of the component medical societies.

ACTION: *Adopted as amended.*

Referred to: Bureau of Research and Planning.

DRIVERS AND SAFETY STANDARDS

Resolution No. 10-67

Committee 3

Introduced by: San Francisco Delegation

WHEREAS, there is a need for non-emergency transportation service for handicapped persons to medical facilities; and

WHEREAS, this is done on doctors' prescription only through services other than conventional ambulances and at a considerable saving to the taxpayer; now, therefore, be it

Resolved: That the CMA request the appropriate state agency, in consultation with the California Highway Patrol, to establish standards for drivers and safety features in such vehicles.

ACTION: *Adopted as amended.*

Referred to: Commission on Community Health Services.

OFFICERS' COMPENSATION

Resolution No. 11-67

Committee 3

Introduced by: San Francisco Delegation

WHEREAS, certain leaders of the medical profession give an extraordinary amount of time to organized medicine and thereby suffer inordinate loss of income to themselves, their families and their associates; now, therefore, be it

Resolved: That the CMA President, President-Elect and Chairman of the Council be adequately and appropriately compensated, as determined by the Council and Finance Committee; and be it further

Resolved: That the Council and Finance Committee investigate the feasibility of developing a compensation program to fulfill the need of compensating other officers and/or commission and committee members.

ACTION: *Above substitute resolution adopted.*

Referred to: Finance Committee.

SUBPOENAS

Resolution No. 12-67

Committee 3

Introduced by: San Francisco Delegation

ACTION: *No action was taken on this resolution.*

CONSERVATION

Resolution No. 13-67

Committee 3B

Introduced by: San Francisco Delegation

WHEREAS, the quality of the environment is critically important to the physical, mental and emotional well-being of people, and

WHEREAS, in many parts of the country, the quality of the environment is being despoiled by air and water pollution, and by destruction of important scenic resources, and

WHEREAS, this matter of environment and its impact on health is of interest to the medical profession as is evidenced by its inclusion in the report of the National Commission on Community Health Services entitled *Health is a Community Affair*; now, therefore, be it

Resolved: That the CMA work through its existing structures to further the work of conservation of natural resources and seek the support of the AMA as well as individual physicians regarding this national problem.

ACTION: *Above substitute resolution adopted.*

Referred to: Commission on Community Health Services, and AMA Delegation.

STUDY OF RVS TO BE CHANGED TO A NOMENCLATURE WITH CODE NUMBERS

Resolution No. 14-67 Committee 3A

Introduced by: Milo A. Youel, M.D.
Representing: San Diego County

WHEREAS, the RVS is readily converted to a fixed fee schedule by applying a conversion factor to the relativity numbers; and

WHEREAS, fixed fee schedules tend to raise the cost of medical care without permitting latitude in individual physicians' fees; and

WHEREAS, the Federal Medicare Program and the State Medi-Cal programs have embraced the usual fee concept for professional services; and

WHEREAS, doctors are anxious to change workmen's compensation fee schedules and other programs with fixed fee schedules to the payment of usual fees; now, therefore, be it

Resolved: That the House of Delegates of CMA direct a study of the effect on the practice of medicine in California that would likely result if the relativity numbers of the Relative Value Studies were deleted, thus changing the Relative Value Studies to a nomenclature with code numbers; and to make recommendations regarding the advisability of making this change.

ACTION: Refer to Council for further study.

Referred to: Commission on Medical Services.

‘ ‘ ‘

CALIFORNIA ABORTION LAW

Resolution No. 15-67 Committee 3

Introduced by: Richard F. Altman, M.D.
Representing: Orange County

ACTION: Not adopted.

‘ ‘ ‘

CPS MEDICAL ADVISORS

Resolution No. 16-67
California Blue Shield Committee

Introduced by: James O. Farley, M.D.
Representing: Tenth District

Resolved: That the system of CPS local medical advisors be utilized to the fullest extent practical in matters of fees and utilization.

ACTION: Above substitute resolution adopted.

Referred to: CPS-Blue Shield Board of Trustees.

‘ ‘ ‘

COMPENSATION STUDY

Resolution No. 17-67 Committee 3

Introduced by: James O. Farley, M.D.
Representing: Tenth District

ACTION: See Resolution No. 11-67 with which this resolution was combined.

AUTHORSHIP OF RESOLUTIONS

Resolution No. 18-67 Committee 3

Introduced by: James O. Farley, M.D.
Representing: Tenth District

WHEREAS, the House of Delegates is made up of Delegates, not delegations, societies, councils or districts; and

WHEREAS, many resolutions are introduced in the name of a delegation, society, council or district; and

WHEREAS, only a delegate can actually introduce a resolution; and

WHEREAS, it is frequently advantageous that the original author of each resolution be known in order to facilitate discussion by local delegations, societies and members with the author prior to or during the meeting of the House of Delegates; and

WHEREAS, resolutions presented in the name of an individual delegate carry a personal responsibility; now, therefore, be it

Resolved: That each resolution introduced to the House of Delegates bear the name of its author in addition to the presently required information.

ACTION: Adopted as amended.

Referred to: Speaker of the House of Delegates and Executive Director.

‘ ‘ ‘

WITNESS FEES

Resolution No. 19-67 Committee 3

Introduced by: Orrin S. Cook, M.D.
Representing: Tenth District

WHEREAS, California law holds that a medical witness, expert or otherwise, can only recover statutory witness fees when so called upon in matters of litigation; and

WHEREAS, numerous other states' statutes provide that such witnesses are legally entitled to the reasonable value of their time; now, therefore, be it

Resolved: That the CMA Committee on Legislation be directed to seek the introduction in the California legislature of appropriate measures which will legally entitle witnesses, whose opinions are elicited as testimony, to be compensated for the reasonable value of their time.

ACTION: Adopted and referred to the Council for implementation.

Referred to: Committee on Legislation.

‘ ‘ ‘

HOUSE FLOOR DEBATE

Resolution No. 20-67 Committee 3

Introduced by: James O. Farley, M.D.
Representing: Tenth District

ACTION: Not adopted.

MEDICARE/MEDI-CAL IDENTIFICATION CARDS

Resolution No. 21-67

Committee 3A

Introduced by: Franklin Murphy, M.D.

Representing: Butte-Glenn Medical Society

WHEREAS, the extension of medical insurance and medical welfare to large numbers of our population has markedly increased the amount of records and paperwork required of the practicing physician; and

WHEREAS, such increased paperwork greatly increases the cost of medical care; and

WHEREAS, proper recording of the patient's name, identification numbers, and other related information are essential for the rapid and accurate processing of such records; now, therefore, be it

Resolved: That the California Medical Association strongly recommend that a plastic identification card with raised letters and numerals be developed and issued by the insurance carriers to each eligible patient; and be it further

Resolved: That all appropriate claim forms and records be designed to permit mechanical imprinting of such card.

ACTION: *Referred to Council for further study.*
Referred to: CPS-Blue Shield Board of Trustees.

1 1 1

IMPLEMENTATION OF TITLE XIX

Resolution No. 22-67

Committee 3A

Introduced by: Burt L. Davis, M.D.

Representing: Santa Clara County

WHEREAS, Public Law 89-97 established Title XIX of the Social Security Laws with the provision that the respective states implement the Title within a few years; and

WHEREAS, the implementation of this Title has been effectuated in a wide variety of ways, some of which appear not to be in the best interests of the health of the beneficiaries; and

WHEREAS, active participation and leadership in the formulation of the state procedures is an obligation of the medical profession in order best to serve our patients; now, therefore, be it

Resolved: That the California Medical Association requests that the American Medical Association advise its constituent societies to take an active part in the legislative processes in their respective states in order to produce workable implementation of Title XIX.

ACTION: *Adopted and referred to the AMA delegation.*

CAMPAIGNING BY NOMINEES FOR MAJOR OFFICES OF CMA

Resolution No. 23-67

Committee 3

Introduced by: Ralph E. Graham, M.D.

Representing: Orange County Delegation

ACTION: *Not adopted.*

1 1 1

EXTENDED CARE FACILITY ADMITTANCE

Resolution No. 24-67

Committee 3A

Introduced by: Orange County Delegation

WHEREAS, Public Law 89-97 (Medicare) now requires a patient to be hospitalized in a licensed general hospital at least three days immediately preceding admittance to an extended care facility; and

WHEREAS, there are many patients whose conditions do not warrant hospitalization in a general hospital, but do need the nursing care and attention provided by an extended care facility; and

WHEREAS, the requirement of three days hospitalization in a general hospital before entering an extended care facility sometimes causes unnecessary hospital bed occupancy and increased cost to the taxpayers; and

WHEREAS, the provisions for participation in the Medicare program by an extended care facility does call for a review of newly admitted patients by a utilization review committee of the facility; and

WHEREAS, the medical decision as to the type of facility in which the patient can best be served is the responsibility of the attending physician; now, therefore, be it

Resolved: That the California Medical Association hereby be instructed to use all its resources, facilities, and influence to have the three day hospitalization in general hospital prior to admittance to an extended care facility, deleted.

ACTION: *Adopted and referred to AMA delegation.*

Referred to: AMA Delegation.

1 1 1

IMPROVED NURSES TRAINING

Resolution No. 25-67

Committee 3

Introduced by: Orange County Delegation

ACTION: *No action was taken on this resolution.*

1 1 1

NURSE-MIDWIFE TRAINING PROGRAM

Resolution No. 26-67

Committee 3

Introduced by: Leon Parrish Fox, M.D.

Representing: Santa Clara County Medical Society

WHEREAS, there is National and State agitation in medical school and public health areas for the

training and utilization of nurse-midwives in pre-natal and maternal care of patients; and

WHEREAS, this would seem to be a retrogressive step in the overall effort to upgrade obstetrical care; and

WHEREAS, the evidence for need of these paramedical personnel is seemingly built on philosophy rather than fact; and

WHEREAS, this proposal would further decimate an already sparse supply of registered nurses who would be trained in midwifery and finally undertake the partial practice of obstetrics; and

WHEREAS, California Business and Professions Code 2140 states, "The certificate to practice midwifery authorizes the holder to attend cases of normal childbirth," and prohibits the licensee from the practice of medicine and surgery as implied in this new proposal; and

WHEREAS, it is apparent that the medical profession is obligated to determine the quantity as well as the quality of true medical care; now, therefore, be it

Resolved: That the Committee on Maternal and Child Care be directed to conduct a comprehensive study concerning the present personnel needs in prenatal and maternity care in California; and be it further

Resolved: That this Committee evaluate the need for nurse-midwives in California and identify the specific function of such personnel in obstetrical practice today; and be it further

Resolved: That this Committee report its findings and recommendations to the House of Delegates at the next annual session.

ACTION: Adopted.

Referred to: Committee on Maternal and Child Care and Commission on Allied Health Professions.

1 1 1

COOPERATION WITH CCHPA

Resolution No. 27-67

Committee 3A

Introduced by: Marin Medical Society

WHEREAS, the stated purpose of the California Council for Health Plan Alternatives is the best possible health care for union members and their families; and

WHEREAS, it could be mutually advantageous to both the CMA and the CCHPA for a relationship to develop which would allow easy communications and the development of a better relationship; now, therefore, be it

Resolved: That the CMA continue its dialogue with the CCHPA without stated commitment.

ACTION: Above substitute resolution adopted as amended and referred to Council.

Referred to: Emergency Action Committee.

SOLID WASTE DISPOSAL

Resolution No. 28-67

Committee 3B

Introduced by: Marin Medical Society

WHEREAS, the production of solid wastes in California is increasing rapidly as a result of population growth and increasing prosperity; and

WHEREAS, the disposal of solid wastes in California has become an urgent problem in environmental health, resulting not only in land pollution, but contributing significantly to the pollution of air through the burning of refuse, and to the pollution of the waters of State through the dumping of refuse and its use as tideland fill; and

WHEREAS, proper solid waste management now requires a level of technology and capital expenditure which can best be provided economically on a regional basis; now, therefore, be it

Resolved: That the California Medical Association through its Committees on Public Health and Environmental Health take strong leadership at the State level to urge and assist in the development of area-wide plans to provide efficient disposal of solid wastes in a manner that will prevent pollution of air, water and land; and be it further

Resolved: That the California Medical Association urge and assist its component societies to take similar action at local levels helping to coordinate local plans for solid waste disposal with area-wide or regional plans where appropriate.

ACTION: Adopted.

Referred to: Commission on Community Health Services and the AMA Delegation.

1 1 1

SMOKING AND THE AMA

Resolution No. 29-67

Committee 3B

Introduced by: Marin Medical Society

WHEREAS, the Council of the CMA has approved a position paper on cigarette smoking and health; now, therefore, be it

Resolved: That our AMA delegates introduce a resolution (1) that the AMA take a stand on cigarette smoking similar to the CMA position, and (2) that the AMA join the National Inter-agency Council on Smoking and Health.

ACTION: Adopted.

Referred to: AMA Delegation.

1 1 1

DELEGATES, LIMITATION OF CONTINUOUS TERMS

Resolution No. 30-67

Committee 3

Introduced by: Marin Medical Society

WHEREAS, the more physicians who participate in Medical Society affairs, the more accurately

will their decisions reflect the current opinions of the majority; and

WHEREAS, the present system of electing Delegates and Alternate Delegates to the CMA and AMA encourages some doctors to participate in those capacities for many years; and

WHEREAS, there are disadvantages to lengthy tenures in that the same minds, year after year, may become fixed on certain issues and less apt to reflect the changing thoughts of both practicing physicians and the public; and

WHEREAS, practicing physicians are often heard to voice displeasure that the CMA and AMA decisions are always made by the same people; now, therefore, be it

Resolved: That the CMA should study the relative merits of limiting the number of continuous terms for Delegates and Alternate Delegates to the AMA.

ACTION: *Adopted as amended.*

Referred to: *Committee on Organizational Review and Planning.*

1 1 1

EXTENDED CARE FACILITY CERTIFICATION

Resolution No. 31-67

Committee 3A

Introduced by: Marin Medical Society

WHEREAS, an Extended Care Facility, as defined in P.L. 89-97, is an entity intended to provide sub-acute care for illnesses which have required hospitalization; and

WHEREAS, there is the implication of *restorative* rather than mere nursing care, since many auxiliary health services are supposed to be available in the Extended Care Facility which were not commonly found in nursing homes; and

WHEREAS, a great number of nursing homes have already been certified as Extended Care Facilities; most of these being the larger institutions which could afford the expenditure of time, money and personnel to meet the requirements of certification; and

WHEREAS, these institutions do not appear to be very materially changed in this process, particularly since they are still mostly filled with the more static Medi-Cal patients; and

WHEREAS, the smaller nursing homes, many of which have done an adequate job with semi-custodial patients, cannot hope to truly meet some of the certification requirements and will be put out of business by the more recent requirement that a facility be certified (for Medicare) by January 1968 if it is to continue eligible for Medi-Cal patients; and

WHEREAS, it now appears that the number of

beds already certified for Extended Care Facilities is in excess of anticipated demands while there is an increasing need of beds for static, often semi-custodial type patients; now, therefore, be it

Resolved: That the California Medical Association voice its disapproval of and seek to change the requirement that Medicare certification be obtained by all nursing homes which care for Medi-Cal patients; and be it further

Resolved: That the California Medical Association urge the State Department of Public Health to certify (or re-certify) as Extended Care Facilities, only those institutions with demonstrated capabilities of *wholly* meeting the conditions of participation; thus making a more clear-cut differentiation between nursing homes (in the older sense) and Extended Care Facilities; and be it further

Resolved: That the California Medical Association carry on an educational program for physicians to better acquaint them with the unique functions of the Extended Care Facility in the spectrum of health care services.

ACTION: *Adopted and referred to Council.*

Referred to: *Ad hoc Committee on Extended Care Facilities and the Committee on Legislation.*

1 1 1

JOURNAL OF THE AMA, AVAILABILITY WITH NO CHARGE TO MEDICAL STUDENTS AND INTERNS

Resolution No. 32-67

Committee 3B

Introduced by: Herman H. Stone, M.D.

Representing: Riverside County Medical Association

ACTION: *Not adopted.*

1 1 1

PROPOSED FORMS, FOR THE INTRODUCTION OF CMA RESOLUTIONS

Resolution No. 33-67

Committee 3

Introduced by: Herman H. Stone, M.D.

Representing: Riverside County Medical Association

WHEREAS, it is becoming exceedingly more difficult each year for the House of Delegates to complete their business because of the increasing number of resolutions introduced; now, therefore, be it

Resolved: That all resolutions when introduced be set forth on line-numbered type paper to enable the Delegates to more easily find the appropriate word, phrase or sentence on the printed page when a specific word, phrase or sentence is referred to.

ACTION: *Adopted as amended.*

Referred to: *Executive Director.*

INTEGRATION AND NURSING CURRICULA

Resolution No. 34-67

Committee 3

Introduced by: C. G. Scarborough, M.D.

Representing: Santa Clara County

WHEREAS, California and the nation are acutely in need of qualified Graduate Nurses; and

WHEREAS, there are now three different types of nursing training courses leading to the licensure of Registered Nurse; and

WHEREAS, each of these three training courses has a slightly different objective goal and therefore somewhat different curriculum requirements; and

WHEREAS, the strictly nursing courses, since they prepare for the same licensure examination, are basically similar; and

WHEREAS, a fairly large part of the curriculum for nursing in the baccalaureate schools is directed toward general academic subjects; and

WHEREAS, advancement in Nursing to supervisory and teaching positions requires a minimum of a baccalaureate degree; and

WHEREAS, there are many highly qualified persons graduating from Hospital Nursing Schools and from Associate in Arts (Junior College) Schools who are excellent candidates for teaching and Supervisory positions, and who would transfer, if transfer to a baccalaureate program were feasible; and

WHEREAS, such transfer to a baccalaureate school entails a large loss of time and practically starting the whole nursing course over because of lack of curriculum integration between the three types of schools; now, therefore, be it

Resolved: That the California Medical Association's House of Delegates direct the appropriate California Medical Association Committee to urge the Health Manpower Council, the Board of Nursing Education and Nurse Registration, and all nursing schools to cooperate in curriculum changes which would permit free transfer of nursing students to baccalaureate programs without undue loss of time or expense thereby increasing the supply of teaching and supervisory courses.

ACTION: Adopted.

Referred to: Commission on Allied Health Professions and the CMA Representatives to the Health Manpower Council.

1 1 1

FOUNDATIONS FOR MEDICAL CARE

Resolution No. 35-67

Committee 3A

Introduced by: Ninth District

ACTION: No action was taken on this resolution.

WEIGHT CONTROL DOCTORS

Resolution No. 36-67

Committee 3B

Introduced by: Ninth District

ACTION: No action was taken on this resolution. See resolution No. 102-67.

1 1 1

CMA COMMITTEE ON EMERGENCY MEDICAL CARE

Resolution No. 37-67

Committee 3

Introduced by: Carl E. Anderson, M.D.

Representing: Santa Rosa

WHEREAS, accidental injuries are the fourth most common cause of death and are the leading cause of death among persons aged 1-37; and

WHEREAS, one-fourth million Californians are injured or killed annually in traffic accidents; and

WHEREAS, injured persons and those suddenly ill require immediate services from an emergency system which involves first-aid, communications, and transportation as well as emergency and definitive medical care; and

WHEREAS, the components of the emergency care system often exist in an unplanned and uncoordinated jumble of unrelated services; and

WHEREAS, many organizations including the AMA, the National Academy of Sciences, the American College of Surgeons, the President's Committee on Traffic Safety and the U.S. Public Health Service have recognized the inadequacies of the emergency care system, and have called for prompt remedial action; and

WHEREAS, there is presently no committee of CMA concerned with the broad problems of the emergency care system; now, therefore, be it

Resolved: That the California Medical Association, through its Council, establish a Committee or Task Force on Emergency Medical Services for the following purposes:

1. Making studies of presently available facilities for emergency medical services in the State of California, including the adequacy and the distribution of such facilities.

2. In cooperation with the California Hospital Association and other interested groups, make recommendations for improving and upgrading emergency medical facilities when they may be found to be inadequate.

3. Maintain liaison with other agencies, governmental and non-governmental for the purpose of improving the entire emergency service system in California; and be it further

Resolved: That the Council be requested to report to the 1968 Session of this House of Dele-

gates, the activities and programs of this public service endeavor.

ACTION: Adopted.

Referred to: Commission on Community Health Services.

‘ ‘ ‘

FINANCING OF THE EMERGENCY MEDICAL CARE SYSTEM

Resolution No. 38-67

Committee 3

Introduced by: Carl E. Anderson, M.D.

Representing: Santa Rosa

WHEREAS, lack of available funds is often one of the major barriers to the development and staffing of adequate ambulance services and of high quality hospital emergency facilities as well as of other segments of the emergency medical care system; and

WHEREAS, an up-to-date emergency care system is important to the public health and safety and could save numerous lives and much disability; and

WHEREAS, gasoline and alcohol are major factors contributing to the need for the emergency medical care system; and

WHEREAS, the State of California annually derives many millions of dollars from taxes on gasoline and alcohol, and uses these monies for diverse purposes; now, therefore, be it

Resolved: That the California Medical Association, through an appropriate committee or committees, study in consultation with other interested organizations, the feasibility of and appropriate mechanisms for the use of some of the State's gasoline and alcohol tax revenues for the purpose of improving the entire system of emergency medical care services.

ACTION: Adopted, referred to Council.

Referred to: Commission on Community Health Services.

‘ ‘ ‘

REPORTING OF BATTERED CHILD

Resolution No. 39-67

Committee 3

Introduced by: Fresno County Medical Society

WHEREAS, tens of thousands of small children yearly are maimed and killed by parental abuse; and

WHEREAS, it is recognized that families of abused children are in need of medical and social services; and

WHEREAS, present California State Law makes reporting of suspected child abuse exclusively a

police matter, thereby causing reluctance to report suspected cases by the physician; and

WHEREAS, a bill regarding the battered child is presently being introduced in the State Legislature by Mr. George Zenovich, Assemblyman of Fresno, which would take child abuse reporting out of the arena of purely law enforcement and place it in the hands of medically oriented social services; now, therefore, be it

Resolved: That the California Medical Association give its full support to the Zenovich Bill, through the Public Health League and education of legislators through all channels available; and be it further

Resolved: That the California Medical Association delegation to the American Medical Association urge similar legislation at state and national levels.

ACTION: Adopted as amended.

Referred to: Committee on Legislation, Public Health League and the AMA Delegation.

‘ ‘ ‘

RESTRICT MEETING TIME TO CMA BUSINESS

Resolution No. 40-67

Committee 3

Introduced by: Fresno County Medical Society

WHEREAS, the sole purpose of the meetings of the House of Delegates of the California Medical Association is to conduct the business of the CMA; and

WHEREAS, the time available for such business is the minimal in which to conduct that business; and

WHEREAS, in recent years there has been a growing tendency to the giving of commendations, awarding of plaques and various awards to members of component societies; now, therefore, be it

Resolved: That further awards and commendations be given at the discretion of the Speaker of the House at such times as not to interfere with the efficient utilization of time.

ACTION: Adopted as amended.

Referred to: Speaker of House of Delegates.

‘ ‘ ‘

CHIROPRACTORS AND MEDICAL

Resolution No. 41-67

Committee 3A

Introduced by: Alameda-Contra Costa Medical Assn.

Resolved: That the California Health and Welfare Agency be urged to remove chiropractors as providers of health services.

ACTION: Adopted as amended and referred to Council.

Referred to: Committee on Legislation.

USUAL AND CUSTOMARY FEES IN WORKMEN'S COMPENSATION

Resolution No. 42-67

Committee 3A

Introduced by: Alameda-Contra Costa Medical Assn.

Resolved: That the Administrative Director of the Division of Industrial Accidents of the Department of Industrial Relations be urged to continue progress in medical economics by adopting the usual and customary fee concept for workmen's compensation cases, and further be it

Resolved: That the Administrative Director also be urged to provide for the free choice of physicians under the Workmen's Compensation Insurance Act.

ACTION: Above substitute resolution adopted and referred to the Council.

Referred to: Industrial Medical Committee.

1 1 1

PKU TESTING

Resolution No. 43-67

Committee 3

Introduced by: Alameda-Contra Costa Medical Assn.

WHEREAS, the yield of treatable cases of PKU from the screening now required by law has not been evaluated to the satisfaction of all properly interested parties; now, therefore, be it

Resolved: That the California State Legislature be urged NOT to make permanent the current PKU Testing Law until such time as a full evaluation can be made and reported.

ACTION: Adopted.

Referred to: Committee on Legislation.

1 1 1

UTILIZATION STUDY OF CLOSED PANELS

Resolution No. 44-67

Committee 3

Introduced by: Alameda-Contra Costa Medical Assn.

WHEREAS, closed panel insurance plans cite publicly their low utilization as compared with that of Blue Cross, Blue Shield and other insurance programs; and

WHEREAS, this low utilization is cited as an indication of a higher quality of medical care and as resulting from "preventive medicine"; and

WHEREAS, most practitioners in areas where closed panel plans exist, care for patients who are subscribers to closed panel plans and the costs for this care are paid to the private practitioners directly by the patient in spite of and without utilization of the pre-paid medical benefits he is entitled to under the closed panel plan; now, therefore, be it

Resolved: That the Bureau of Research and Planning be ordered by this House to make a study of non-utilization of closed panel plans which

results from a patient's preference for a private practitioner.

ACTION: Adopted.

Referred to: Bureau of Research and Planning.

1 1 1

COMMENDATION OF CPS

Resolution No. 45-67

California Blue Shield Committee

Introduced by: Alameda-Contra Costa Medical Assn.

Resolved: That California Physicians' Service be commended for the responsiveness it has shown to physician problems during the burdensome year it has shouldered the task of being the fiscal agent for Medi-Cal.

ACTION: Adopted.

1 1 1

MEDI-CAL PAYMENTS IN TEACHING HOSPITALS

Resolution No. 46-67

Committee 3A

Introduced by: Alameda-Contra Costa Medical Assn.

WHEREAS, the medical profession has been charged with the responsibility of safeguarding the reasonableness of costs for physicians' services in the Medicare and Medi-Cal programs; now, therefore, be it

Resolved: That the House of Delegates of the California Medical Association recommends to the administrators of the Medicare and Medi-Cal Programs and to their fiscal intermediaries the following criteria for payment of Medicare and Medi-Cal claims in teaching hospitals:

1. For doctors not on salary in teaching hospitals payment should be made only to individual physicians who actually render medical care to Medicare or Medi-Cal patients, upon receipt of individual bills from each doctor for each individual service rendered by them.

2. The amount of payment should be commensurate with the value of the actual service rendered the patient by the billing physician.

3. When services are rendered to Medicare and Medi-Cal patients by salaried physicians in a teaching hospital, payment by Medicare and Medi-Cal should not exceed that percentage of each doctor's salary which can be equitably allocated to his services to Medicare and Medi-Cal patients.

4. Total cost to Medicare and Medi-Cal for physician services to a Medicare or Medi-Cal patient in a teaching hospital, including costs charged to the program for interns, residents, and full-time physicians and visiting staff, should not exceed costs which the program would be obligated to pay if the patient had been under private care.

ACTION: Referred to Council.

AMBULANCE AND EMERGENCY TRAINING

Resolution No. 47-67

Committee 3

Introduced by: Alameda-Contra Costa Medical Assn.

Resolved: That the California Medical Association lead efforts to raise standards for the operation of ambulance and other emergency services and the qualifications of ambulance personnel through educational and administrative assistance to training groups on the local level.

ACTION: *Adopted.*

Referred to: *Commission on Community Health Services.*

1 1 1

CRIPPLED CHILDREN'S PROGRAM

Resolution No. 48-67

Committee 3A

Introduced by: Alameda-Contra Costa Medical Assn.

WHEREAS, the Medi-Cal program now provides state funds to pay for the full spectrum of medical services, including services of specialists for indigent and medically indigent children; and

WHEREAS, preservation of the separate administration of Crippled Children's Service Program not only constitutes a duplication of available services to children but also imposes administrative hindrances, unnecessary complexities and unnecessary expense in the processing of claims for services rendered to children; now, therefore, be it

Resolved: That this House of Delegates express its conviction that handling of claims for physicians' services under Crippled Children's Service to be merged with those of the Medi-Cal program, using the same fiscal intermediary and the same "usual and customary fee" basis for payment; and be it further

Resolved: That CMA study and promote further merging of these two overlapping programs for medical services to children to the end that the adverse philosophies of panel practice and prior authorization will be eliminated.

ACTION: *Referred to Council with motion to amend by eliminating the second resolved portion.*

1 1 1

NURSING HOME PAYMENTS

Resolution No. 49-67

Committee 3A

Introduced by: Alameda-Contra Costa Medical Assn.

Resolved: That Medi-Cal be urged to devise a system of payment which will properly compensate nursing homes in accordance with the degree of care needed by and provided to the patient.

ACTION: *Adopted and referred to the Council for implementation.*

Referred to: *Commission on Public Agencies.*

DISCLOSURE OF SOURCE OF FUNDS

Resolution No. 50-67

Committee 3

Introduced by: Alameda-Contra Costa Medical Assn.

Resolved: That if the Bureau of Research and Planning is subsidized in carrying out studies, research or questionnaires by Federal, State or other agencies which are not part of the California Medical Association, the source of such outside funds and the ultimate disposition of the report and study results be clearly pointed out to California Medical Association members asked to participate.

ACTION: *Adopted.*

Referred to: *Bureau of Research and Planning.*

1 1 1

TOWN-GOWN LIAISON

Resolution No. 51-67

Committee 3B

Introduced by: C. Gerald Scarborough, M.D.

Representing: Santa Clara County Delegation

WHEREAS, the quality of medical care of the future which is of mutual concern to medical educators and practicing physicians is dependent to a large degree on present medical education; and

WHEREAS, there are numerous local problems and circumstances peculiar to each medical school and geographic area; now, therefore, be it

Resolved: That the CMA urge those component medical societies which have geographic proximity to a medical school and which do not have a liaison committee to consider the creation of such a committee.

ACTION: *Above substitute resolution adopted.*

Referred to: *Liaison Committee to Medical Schools.*

1 1 1

FREE CIGARETTES

Resolution No. 52-67

Committee 3B

Introduced by: C. Gerald Scarborough, M.D.

Representing: Santa Clara County Delegation

ACTION: *Not adopted.*

1 1 1

TODAY'S HEALTH GUIDE

Resolution No. 53-67

Committee 3B

Introduced by: C. Gerald Scarborough, M.D.

Representing: Santa Clara County Delegation

WHEREAS, pertinent health information is presented in a well organized, easily read, and clearly illustrated book entitled *Today's Health Guide*; and

WHEREAS, this book could be used as a text for health and family life education in our public and private schools; now, therefore, be it

Resolved: That the California Medical Association through its component medical societies

(1) encourage wider distribution of *Today's Health Guide* in all hospital and school libraries and in all physicians' reception rooms, and (2) give widespread publicity to the desirability of having every family obtain a copy.

ACTION: *Above substitute resolution adopted.*

Referred to: *Commission on Community Health Services and Commission on Communications.*

1 1 1

PROTECTIVE HELMETS FOR MOTORCYCLISTS

Resolution No. 54-67

Committee 3B

Introduced by: San Mateo County Delegation

WHEREAS, the number of motorcycle deaths are increasing each year; and

WHEREAS, two-thirds to three-fourths of the deaths in these accidents are due to head injuries; and

WHEREAS, the wearing of safety helmets can reduce the risk of fatality in a motorcycle accident to about one-third of the risk without a helmet; and

WHEREAS, several states have already passed legislation requiring motorcyclists to wear safety helmets; and

WHEREAS, legislation has been introduced in the present session of the State Legislature, which would require motorcycle operators to wear a protective helmet of a type approved by the California Highway Patrol; now, therefore, be it

Resolved: That the California Medical Association give its endorsement to legislation which requires all motorcyclists to wear properly designed protective headgear; and be it further

Resolved: That the CMA pursue an active role in stimulating and supporting other legislation which provides safeguards for motorcycle operators and pedestrians.

ACTION: *Above substitute resolution adopted.*

Referred to: *Commission on Community Health Services and Legislative Committee.*

1 1 1

USE OF MARIJUANA, LSD AND OTHER HALLUCINATORY DRUGS

Resolution No. 55-67

Committee 3B

Introduced by: San Mateo County Delegation

WHEREAS, the use of Marijuana, LSD and other hallucinatory drugs is rapidly increasing particularly by those young adults still in high school and college; and

WHEREAS, the user of these drugs has little factual knowledge as to their pharmacological and psychiatric effects and rely upon nonprofessionals for information; and

WHEREAS, probably even less is known about these drugs by the majority of the medical profession who should be the best informed; and

WHEREAS, school, Church and civic groups are looking to the medical profession for instruction and guidance as to the handling of the problems generated by the use of these drugs; and

WHEREAS, organized medicine should take the lead in providing both information for the public in general regarding the use of these drugs and also should educate physicians so they will be more knowledgeable as to the effects of hallucinatory drugs; now, therefore, be it

Resolved: That the California Medical Association:

1. Continue to provide and expand educational programs for the medical profession to learn authoritatively about the various hallucinatory drugs, and

2. Continue to provide and expand techniques to educate the public as to the pharmacological and psychological effects of hallucinatory drugs.

ACTION: *Adopted as amended.*

Referred to: *Scientific Board.*

1 1 1

CREDIT CARDS FOR MEDICARE AND MEDICAL

Resolution No. 56-67

Committee 3A

Introduced by: Robert J. O'Neill, M.D.

Representing: Santa Clara County

WHEREAS, the medical profession recognizes that CPS has been doing an excellent job of reviewing and paying claims for Medicare and Medical; and

WHEREAS, the greatest difficulty up to this stage has been the question of eligibility; and

WHEREAS, the question of eligibility usually is due to the misspelling of a name, transposition of 14 digit numbers; and

WHEREAS, the medical profession and hospitals would be willing to purchase a credit card stamping machine in order to eliminate some of the delays in payment; now, therefore, be it

Resolved: That this House of Delegates encourage the State of California and local county welfare departments to issue credit cards that may be stamped on medical claim forms in medical offices and hospitals; and be it further

Resolved: That the Social Security Administration be encouraged to issue similar credit cards to Medicare recipients.

ACTION: *Referred to Council for further study.*

Referred to: *CPS-Blue Shield Board of Trustees.*

REGULATION ON BLOOD DONATIONS

Resolution No. 57-67

Committee 3

Introduced by: Robert J. O'Neill, M.D.

Representing: Santa Clara County

ACTION: No action taken.

1 1 1

RELATIVE VALUE STUDIES

Resolution No. 58-67

Committee 3A

Introduced by: Santa Barbara Delegation

WHEREAS, the Relative Value Studies (RVS) has become an invaluable tool of communication in the Medi-Cal Program; and

WHEREAS, the last revision of the RVS took place in 1964, before the initiation of Medi-Cal; and

WHEREAS, certain inequities have become evident in the use of the RVS in this program, to wit:

1. Herniorrhaphy compared with simple appendectomy.

2. Obstetrical procedures including particularly normal delivery with prenatal and postnatal care compared with simple appendectomy.

3. Certain ophthalmological procedures.

4. IPPB

5. Nursing home visits by internists both multiple and intermediate value type; now, therefore, be it

Resolved: That the House of Delegates of the CMA direct that the foregoing specific items be incorporated in the ongoing revision of the Relative Value Studies.

ACTION: Referred to the Committee on Fees.

1 1 1

MEDICAL ETHICS

Resolution No. 59-67

Committee 3B

Introduced by: Santa Barbara Delegation

ACTION: No action was taken on this resolution.

1 1 1

COVERAGE FOR OUTPATIENT DIAGNOSTIC PROCEDURES

Resolution No. 60-67

Committee 3A

Introduced by: San Mateo County Delegation

WHEREAS, health insurance which requires hospitalization in order to receive benefits for diagnostic procedures accentuates the existing shortage of hospital beds and unnecessarily increases the cost of medical care; now therefore, be it

Resolved: That the voluntary health insurance industry be encouraged to develop programs which will provide payments for diagnostic procedures on an out-patient basis.

ACTION: Above substitute resolution adopted.

Referred to: Commission on Medical Services.

1 1 1

MEDICAL SUPERVISION OF BLOOD BANKING DURING UNSCHEDULED, EMERGENCY BLOOD COLLECTIONS

Resolution No. 61-67

Committee 3

Introduced by: Fresno County Medical Society

WHEREAS, blood banking is an integral indispensable facet of medical practice; and

WHEREAS, the direction and supervision of this medical service should properly be the responsibility of physicians; and

WHEREAS, California registered nurses and licensed clinical laboratory technologists, specifically trained in blood banking techniques, carry out the procedures directed and supervised by physicians; and

WHEREAS, physician supervision of licensed, competent and specifically trained nurses and clinical laboratory technologists in general medical parlance does not imply constant, *immediate physical presence* of the physician during performance of specifically delegated procedures; and

WHEREAS, the California Department of Public Health administrative regulations in this regard are unduly restrictive and not in conformity with general medical concepts; Reference California Administrative Code, Title 17, Chapter 11, Sub-Chapter 1, Group 1, Section 998(b), "All blood collection shall take place under the direct and immediate supervision of an attending physician.", and Section 1002(d), "The attending physician . . . shall be immediately available at all times blood collection is carried on."; and

WHEREAS, the American Association of Blood Banks *Standards for a Blood Transfusion Service*, 4th Ed., 1966, Section 1, A and B, and Section 11, B, and the National Institute of Health regulations: Reference Section 73.301(a), and Section 73.302(a), *Public Health Service Publication No. 437*, Revised, 1965 and November 1966, do not narrowly and restrictively construe the meaning of physician direction and supervision; now, therefore, be it

Resolved: That the Council of the California Medical Association through its appropriate commissions and committees be directed to consult with and advise the California Department of Public Health in this regard to allow more flexible

and realistic latitude in the administrative regulations to the end that "medical supervision" not be construed to require the *immediate physical presence* of a physician during the performance of specifically designated blood banking procedures by authorized, licensed and specifically trained California registered nurses and licensed clinical laboratory technologists during unscheduled emergency blood collections.

ACTION: Adopted.

Referred to: Committee on Blood Banks and the Commission on Public Agencies.

1 1 1

MEDICARE LABORATORY REGULATIONS

Resolution No. 62-67

Committee 3A

Introduced by: Glenn A. Pope, M.D.

Representing: Sacramento County

WHEREAS, qualified physicians of various disciplines frequently serve as directors of well supervised laboratories under the licensure of the State of California, and

WHEREAS, regulations have been established by the Department of Health Education and Welfare which will impair the functions of such laboratories operated by physicians or groups of physicians for the benefit of their patients and the patients of other physicians; now, therefore, be it

Resolved: That the California Medical Association review the regulations and strive to correct the inequities in the regulations so that all California laboratories operated by qualified physicians which maintain high standards of proficiency may continue to serve Medicare recipients as well as all other categories of patients in California, and further be it

Resolved: That clinical laboratory services provided by a physician providing no other services to the patient are no less medical services than similar services rendered by physicians providing other services and those medical laboratory services should be regulated in the same manner as are all other services, and further be it

Resolved: That the California Delegates to the American Medical Association be requested to propose an appropriate similar resolution to the next American Medical Association House of Delegates meeting.

ACTION: Above substitute resolution adopted and referred to the Council.

Referred to: Commission on Public Agencies and the AMA Delegation.

HEALTH MANPOWER GUIDELINES

Resolution No. 63-67

Committee 3B

Introduced by: Thomas Elmendorf, M.D.

Representing: Tenth District

WHEREAS, there is a need for increased health manpower; and

WHEREAS, medical schools are developing programs for training specialized personnel to cooperate with physicians and increase their efficiency; and

WHEREAS, trained specialists already exist in ancillary fields such as optometry, podiatry, and clinical psychology; and

WHEREAS, the California Health Manpower Council is currently evaluating manpower programs for these and similar fields; now, therefore, be it

Resolved: That this House of Delegates instruct the appropriate committee of the CMA to interpret ethical relationships and establish guidelines for efficient cooperation between medicine and specialized allied professional personnel in optometry, podiatry, clinical psychology and such other ancillary groups as deemed appropriate by said committee.

ACTION: Adopted.

Referred to: Commission on Allied Health Professions.

1 1 1

FAMILY PHYSICIANS TRAINING

Resolution No. 64-67

Committee 3B

Introduced by: Nathan Dubin, M.D.

Representing: Tenth District

WHEREAS, good medical care has always been based on the availability, competence and personal patient relationships of family physicians; and

WHEREAS, medical schools are graduating fewer general practitioners on the premise that greater specialization is being made necessary by the increasing amount and complexity of medical knowledge; and

WHEREAS, the trend toward highly specialized medical practice has produced an increased demand of the public for comprehensive medical care; now, therefore, be it

Resolved: That the California Medical Association commend those medical schools which are exploring or implementing ways to attract and train physicians in the field of General Practice, and be it further

Resolved: That those medical schools that have not as yet contemplated or embarked upon such programs be urged to provide their students with more adequate information and greater encouragement concerning family practice as a professional career, and be it further

Resolved: That the appropriate CMA Committee, through liaison efforts, keep itself informed of various developments and progress made in achieving the above, and that a progress report be submitted to the House of Delegates at its next annual convention.

ACTION: *Above substitute resolution adopted as amended.*

Referred to: *Scientific Board and Liaison Committee to Medical Schools.*

‘ ‘ ‘

MEDICAL CARE FORM REVIEW

Resolution No. 65-67

Committee 3A

Introduced by: Franklin Murphy, M.D.

Representing: Butte-Glenn County

Resolved: That a committee of the Commission on Medical Services be established to develop and promote the use of a standard reporting form for private and government third party payment programs; and be it further

Resolved: That this committee study and represent the physicians of California in the broad field of automation and data processing, including the processing of claims for physicians' services to the end that the needs of physicians will be properly recognized in the programming of this rapidly developing facet of medical economics.

ACTION: *Above substitute resolution adopted and referred to Council.*

Referred to: *Commission on Medical Services.*

‘ ‘ ‘

RECIPROCITY CERTIFICATION

Resolution No. 66-67

Committee No. 3B

Introduced by: Monterey County Delegation

WHEREAS, the Medical Profession has always been a dignified one and the licensing certificate should reflect this dignity; and

WHEREAS, the appearance of the words "Reciprocity Certificate" stamped diagonally across the medical license issued by reciprocity by the California State Board of Medical Examiners detracts from the dignity of the certificate; and

WHEREAS, the wording of the certificate clearly identifies it as having been granted by reciprocity; now, therefore, be it

Resolved: That the California Medical Association go on record as favoring the removal of the words "Reciprocity Certificate" stamped diagonally across the medical licenses so issued; and be it further

Resolved: That this resolution be referred to the Council for appropriate action.

ACTION: *Referred to Council.*

Referred to: *Board of Medical Examiners.*

EXTENDED CARE FACILITIES

Resolution No. 67-67

Committee 3A

Introduced by: San Francisco Delegation

WHEREAS, there is a massive effort by the administrators of nursing home and extended care facilities to bring their facilities into compliance with the "Conditions of Participation for Extended Care Facilities" of the U.S. Department of HEW (Social Security Administration pamphlet HIM-3) and have indicated willingness to be guided by physician committees in matters concerning the quality of medical care in their institutions; and

WHEREAS, "Conditions of Participation for Extended Care Facilities" do not suggest or include any discussion of the relation of the facility to a medical staff committee or organization; and

WHEREAS, utilization problems and other medical staff functions could best be guided by a local medical society equivalent staff committee when the staff is small; now, therefore, be it

Resolved: That the CMA find and promote ways of implementing the Guiding Principles concept into extended care facility development and that the CMA encourage its component societies to participate actively in staff supervision activities in the facilities in their communities.

ACTION: *Adopted.*

Referred to: *Ad hoc Committee on Extended Care Facilities.*

‘ ‘ ‘

OPPOSITION TO SENATE BILL 260

Resolution No. 68-67

Committee 3B

Introduced by: John A. Bullis, M.D.

Representing: Los Angeles

ACTION: *No action was taken on this resolution.*

‘ ‘ ‘

PHYSICAL EVALUATION OF CLASS I AND II DRIVERS

Resolution No. 69-67

Committee 3B

Introduced by: Ralph M. King, M.D.

Representing: San Diego Delegation

WHEREAS, the California State Department of Motor Vehicles has established a classification for the operators of heavy rigs (trucks and buses) that operate on the highways of the state; and

WHEREAS, the medical evaluation required for the issuance of licenses to the operators of such vehicles is to be conducted by the applicant's personal physician; and

WHEREAS, it is recognized that examinations such as one on which the means of earning a livelihood may depend can create an area of conflict and emotional unrest and potential deterioration of normal doctor-patient relationship; and

WHEREAS, the California Society of Internal

Medicine has approved a similar resolution in its last House of Delegates; now, therefore, be it

Resolved: That the California Medical Association recommend that the Department of Motor Vehicles designate independent medical examiners for class I and II drivers' licenses; and be it further

Resolved: That the California Medical Association and its component medical societies offer assistance to the DMV in the accomplishment of this program.

ACTION: Adopted.

Referred to: Commission on Community Health Services.

1 1 1

RECOGNITION OF AN OUTSTANDING EFFORT

Resolution No. 70-67

Committee 3B

Introduced by: E. Kash Rose, M.D.

Representing: Ninth District

WHEREAS, Dr. Carl Anderson has officially announced his retirement as Councilor of the Ninth District and therefore necessarily as Chairman of the Council; and

WHEREAS, Dr. Anderson for the past seven years has given of himself so extensively and unselfishly above and beyond that of most physicians; and

WHEREAS, Dr. Anderson's contributions to the Ninth District, CMA and AMA have been of such magnitude that no quality control is needed; now, therefore, be it

Resolved: That this House of Delegates commends Dr. Anderson and expresses its deepest appreciation for his many efforts over the past seven years as Councilor and six years as Chairman of the Council.

ACTION: Adopted.

Referred to: Commission on Communications.

1 1 1

MEDI-CAL DRUG FORMULARY

Resolution No. 71-67

Committee 3A

Introduced by: C. Gerald Scarborough, M.D.

Representing: Santa Clara County

Resolved: That this House of Delegates of the California Medical Association endorses the principle that any drug formulary short of a listing of all of the drugs various physicians find necessary for the treatment of all of their patients is by its nature restrictive and inhibits the proper treatment of patients; and, further, be it

Resolved: That the California Medical Association take all possible steps to eliminate the drug formulary under the Medi-Cal program.

ACTION: Above substitute resolution adopted.

Referred to: Commission on Public Agencies.

RADIOLOGICAL CONSULTATION

Resolution No. 72-67

Committee 3A

Introduced by: Los Angeles County Medical Association

WHEREAS, there are at least two clearly defined categories of x-ray examinations:

1. Those accomplished by the attending physician incident to other services,

2. Examinations accomplished by other doctors on patients referred by the attending physician for radiological consultation only and including a written report to the referring physician; and

WHEREAS, the historical assumption of the more frequently involved consulting specialists that their services were recognized by their colleagues and knowledgeable interested parties has been challenged in important places including the Joint Committee on Accreditation of Hospitals and the Bureau of Health, Education and Welfare; now, therefore, be it

Resolved: That when a patient is referred for x-ray examination and written evaluation to a doctor not providing therapeutic services to the patient this should be considered by all interested parties a "radiological consultation."

ACTION: Adopted as amended.

Referred to: AMA Delegation.

1 1 1

LEGISLATIVE IMPLEMENTATION OF TITLE XIX, P.L. 89-97

Resolution No. 73-67

Committee 3A

Introduced by: Frank A. Rogers, M.D.

Representing: Los Angeles County Medical Association

ACTION: No action was taken on this resolution.

1 1 1

OPPOSING SENATE BILL S260

Resolution No. 74-67

Committee 3B

Introduced by: Los Angeles County Medical Association

ACTION: No action was taken on this resolution.

1 1 1

FEDERAL SUBSIDIES

Resolution No. 75-67

Committee 3

Introduced by: Frank A. Rogers, M.D.

Representing: Los Angeles County Medical Association

WHEREAS, federal grant money has been accepted in behalf of the California Medical Association by its Council and spent on studies at the direction of the Council; and

WHEREAS, the question has been raised as to the necessity of accepting these funds; now, therefore, be it

Resolved: That the House of Delegates of the California Medical Association in regular session

April 1967 hereby request the Council to use discretion in requesting or accepting further federal subsidies.

ACTION: *Adopted as amended.*
Referred to: Council.

* * *

ADMISSION PROCEDURES TO GENERAL HOSPITALS

Resolution No. 76-67 **Committee 3A**

Introduced by: Leonard M. Asher, M.D.

Representing: Los Angeles County Medical Association

WHEREAS, the patient load in many large general medical hospitals has increased during the past year; and

WHEREAS, available beds for admission of emergency cases has been proportionately reduced by this increased load; and

WHEREAS, it is the responsibility of the medical profession to provide prompt quality medical care on all occasions; now, therefore, be it

Resolved: That the California Medical Association carry out a study of hospital admission procedures in an effort to establish guidelines for hospitals to create more available beds for such emergency admissions.

ACTION: *Adopted.*
Referred to: Commission on Hospital Affairs.

* * *

PRACTICE, ATTEMPT TO PRACTICE WITHOUT A LICENSE, A FELONY

Resolution No. 77-67 **Committee 3**

Introduced by: Los Angeles County Medical Association

WHEREAS, the Healing Arts Section of the Business and Professions Code, now provides that the practicing or attempting to practice, or holding themselves as practicing, any system or mode of treating the sick or afflicted in this state, without an unrevoked certificate as provided in the chapter on Healing Arts, is a misdemeanor; and

WHEREAS, that this Section of the Business and Professions Code is being violated repeatedly by persons not holding an unrevoked certificate, and where such violations are willful and under circumstances or conditions which could cause great bodily harm or serious mental illness, to the sick and afflicted; and

WHEREAS, the punishment provided under the misdemeanor section of the present law is not severe enough to act as a deterrent; now, therefore, be it

Resolved: That the House of Delegates of the California Medical Association instruct the Council of the California Medical Association, acting through its Liaison Committee with the Public Health League, cause to be introduced an Amend-

ment to Section 2141 of the Business and Professions Code to amend said Section to read as follows:

"Any person, who practices or attempts to practice, or who advertises or holds himself out as practicing, any system or mode of treating the sick or afflicted in this state, or who diagnoses, treats, operates for, or prescribes for any ailment, blemish, deformity, disease, disfigurement, disorder, injury, or other mental or physical condition or any person without having at the time of so doing a valid unrevoked certificate as provided in this chapter, is guilty of a felony."

ACTION: *House voted to support the bill called for in this resolution.*

Referred to: Committee on Legislation.

* * *

PROCEDURE FOR DISTRICT WITHDRAWAL FROM COUNTY MEDICAL SOCIETY

Resolution No. 78-67 **Committee 3**

Introduced by: Los Angeles County Medical Association

WHEREAS, no well defined and orderly procedure exists for an established component society to withdraw from its parent County Medical Society and become autonomous; now, therefore, be it

Resolved: That the Speaker of the House of Delegates be hereby authorized to appoint an ad hoc committee of this House of Delegates to study and investigate the problem of the establishment of an orderly procedure for an established component district of a county medical society to exercise option to withdraw from the county medical society and become autonomous and said ad hoc committee to submit a proposed bylaw amendment to the California Medical Association Bylaws that would detail and provide such an orderly procedure.

ACTION: *Adopted.*
Referred to: Speaker of the House of Delegates.

* * *

INCOME TAX DEDUCTION FOR MEDICAL CARE

Resolution No. 79-67 **Committee 3**

Introduced by: Los Angeles County Medical Association

WHEREAS, first dollar deduction from the income tax for medical care is not allowed either by the Federal Government or the State of California; and

WHEREAS, the maintenance of an individual's health (i.e., his equipment) is of great importance in enabling him to earn a living; and

WHEREAS, the maintenance of an individual's health is the maintenance of the equipment with which he works; comparable with the maintenance of industrial equipment for which industry is al-

lowed first dollar deduction from the income tax for the maintenance thereof; and

WHEREAS, an increased burden has fallen upon the younger population to maintain the health of the aged, under Medicare; and

WHEREAS, the younger person is not presently entitled to first dollar deduction from the income tax for his own health, under current laws; now, therefore, be it

Resolved: That the California Medical Association urge and petition the Congress of the United States, through the American Medical Association, and the California Legislature to remove the restriction on first dollar deduction from the income tax, for health expenditure—for physician services, hospitalization, nursing care, physical therapy and prescription drugs.

ACTION: Adopted.

Referred to: Committee on Legislation.

1 1 1

TECHNIQUE TO EXPEDITE USE OF DIRECT PAYMENT PROCEDURE UNDER MEDICARE

Resolution No. 80-67

Committee 3A

Introduced by: Los Angeles County Medical Association

WHEREAS, it is established policy of the California Medical Association to urge all doctors to bill patients directly for services rendered; and

WHEREAS, the patient who has paid for coverage under Part B of Title XVIII can be reimbursed according to the terms of that coverage upon presentation to the carrier of a receipted bill which properly identifies the service rendered; and

WHEREAS, many receipted bills have failed to identify the service rendered so that the carrier could not reimburse the patient until the necessary information was obtained; and

WHEREAS, this delay in reimbursement has caused the frustrated patient to waste the time of the doctor and his staff with endless queries, to correspond repeatedly with the carrier, and finally to appeal directly to his congressman; and

WHEREAS, these expressions of dissatisfaction might lead to a change in the law so that physicians could no longer elect this method of payment; now, therefore, be it

Resolved: That the California Medical Association immediately use all practical methods to expedite the inclusion of all pertinent data on each receipted bill for use under Title XVIII, to wit: patient's name, address with zip code number, identification number, date and place of service, description of service with RVS procedure number, fee, physician's name, address with zip code number, and license number; and be it further

Resolved: That each doctor and his staff be urged to give to any Medicare patient the necessary assistance in filling out the claim form which the patient submits for reimbursement.

ACTION: Adopted.

Referred to: Commission on Communications.

1 1 1

HEALTH INSURANCE FOR INDIVIDUALS OVER 65

Resolution No. 81-67

Committee 3A

Introduced by: Los Angeles County Medical Association

WHEREAS, The California Medical Association has consistently advocated and supported voluntary health insurance as the most desirable and efficient means of providing for large and unforeseen medical and hospital expenses, and

WHEREAS, since the advent of Medicare those of 65 and over have to a large measure been denied the opportunity to continue to provide for themselves through private insurance plans; now, therefore, be it

Resolved: That the California Medical Association endorses the principle of provision of private insurance for those over 65 to allow them a choice; and further, be it

Resolved: That the California Medical Association encourage the health insurance industry, including California Blue Shield, to provide such voluntary health insurance.

ACTION: Above substitute resolution adopted.

Referred to: Commission on Medical Services.

1 1 1

CERTIFICATION AND RECERTIFICATION

Resolution No. 82-67

Committee 3A

Introduced by: Los Angeles County Medical Association

Resolved: That the House of Delegates of the California Medical Association endorses all efforts to repeal the certification and recertification provisions of P.L. 89-97; and be it further

Resolved: That the California Medical Association Delegates to the American Medical Association be instructed to submit a similar resolution to the American Medical Association House of Delegates.

ACTION: Adopted.

Referred to: AMA Delegation.

1 1 1

INDEPENDENT LABORATORIES

Resolution No. 83-67

Committee 3A

Introduced by: Robert Stragnell, M.D.

Representing: Los Angeles County Medical Association

ACTION: See resolution No. 62-67 with which this resolution was combined.

DIRECT PATIENT BILLING

Resolution No. 84-67

Committee 3A

Introduced by: Neal C. Hamel, M.D.

Representing: Los Angeles County Medical Association

WHEREAS, direct patient billing is not now possible under Title XIX, P.L. 89-97 (Medi-Cal); and

WHEREAS, direct patient billing for Medi-Cal patients would be a desirable option for California physicians; now, therefore, be it

Resolved: That the California Medical Association House of Delegates recommend that the option for direct patient billing of Medi-Cal patients is allowed California physicians; and be it further

Resolved: That the California Medical Association Council take whatever action is necessary to encourage legislative and/or regulatory changes which will make possible the desirable option of direct patient billing for Medi-Cal patients.

ACTION: Adopted.

Referred to: Commission on Communications and Committee on Legislation.

‘ ‘ ‘

DIRECT PATIENT BILLING

Resolution No. 85-67

Committee 3A

Introduced by: Los Angeles County Medical Association

Resolved: That the CMA through its various media of communication continue to inform physicians of the importance of the principle involved in direct billing and of the option of direct billing under Medicare.

ACTION: Above substitute resolution adopted.

Referred to: Commission on Communications.

‘ ‘ ‘

INHALATION THERAPY

Resolution No. 86-67

Committee 3B

Introduced by: Frank A. Rogers, M.D.

Representing: Los Angeles County Medical Association

WHEREAS, Inhalation Therapy is an important aspect of medical practice requiring specialized knowledge, training, and technical experience; and

WHEREAS, improved standards in methods of administering Inhalation Therapy together with improved standards in the training of technical paramedical personnel are being developed; and

WHEREAS, medical supervision of Inhalation Therapy practices is an acknowledged necessity; now, therefore, be it

Resolved: That the CMA Council, through an appropriate committee, study the problem and explore the advisability of establishing a special committee in order to achieve the objectives of the resolution, and be it further

Resolved: That the California Delegation to the AMA pursue a similar procedure to achieve the purpose of the resolution.

ACTION: Adopted as amended.

Referred to: Scientific Board and AMA Delegation.

‘ ‘ ‘

DISABILITY INSURANCE PROGRAM

Resolution No. 87-67

Committee 3B

Introduced by: Joseph F. Boyle, M.D.

Representing: Los Angeles County Medical Association

ACTION: No action was taken on this resolution.

‘ ‘ ‘

WEIGHT REDUCTION PRACTICES

Resolution No. 88-67

Committee 3B

Introduced by: Leonard Asher, M.D.

Representing: Los Angeles County Medical Association

ACTION: No action was taken on this resolution. See resolution 102-67.

‘ ‘ ‘

COUNTY SOCIETY AFFILIATIONS

Resolution No. 89-67

Committee 3B

Introduced by: Bernard Axelrod, M.D.

Representing: Los Angeles County Medical Association

ACTION: No action was taken on this resolution.

‘ ‘ ‘

HOSPITAL ACCREDITATION REQUIREMENT

Resolution No. 90-67

Committee 3B

Introduced by: R. S. Neuenschwander, M.D.

Representing: Los Angeles County Medical Association

WHEREAS, the physician's care of a hospitalized patient is succinctly, precisely and completely delineated in the hospital chart by the history, physical examination, orders, operative and progress notes; and

WHEREAS, therapy, intended procedures and details regarding follow-up visits following the discharge of the patient from the hospital are neither properly part of, nor pertinent to the hospital chart; and

WHEREAS, responsibility for continuity of high quality medical care is a function of the medical staff of the individual hospital; and

WHEREAS, the utilization review procedure depends not upon review of a summary of a chart, but rather upon the day-to-day care and progress of the patient, and such review should never be postponed until the patient has been discharged from the hospital; and

WHEREAS, summarization of charts on a routine basis consumes much valuable physician time that might be better utilized in more fruitful, worthwhile and advantageous activities; and

WHEREAS, summarization of a chart neither improves the care rendered that particular patient,

nor greatly alters the care rendered to some future patient in like circumstances; and

WHEREAS, the example of "adequate discharge summary" contained in Bulletin No. 43 of the Joint Commission on the Accreditation of Hospitals is a copying of material that any intelligent individual could easily read from the chart proper in a very few minutes; and

WHEREAS, the requirement of discharge summaries as a basis for the accreditation of hospitals by the Joint Commission on the Accreditation of Hospitals is an unreasonable extension of authority into the rights, responsibilities and ethics of the Medical Profession; now, therefore, be it

Resolved: That the American Medical Association be directed to inform the Joint Commission on the Accreditation of Hospitals that we are unalterably opposed to the requirement of routine discharge summaries for patients' clinical records; and be it further

Resolved: That said Commission be directed to rescind this requirement for the accreditation of hospitals and to instruct its surveyors and all hospitals that such summaries are not a requirement for accreditation.

ACTION: *Referred to Council for further study.*
Referred to: Commission on Hospital Affairs.

1 1 1

COMPULSORY GENERIC PRESCRIBING

Resolution No. 91-67

Committee 3B

Introduced by: Los Angeles County Medical Association

Resolved: That the California Medical Association in regular session assembled April 1967, hereby makes known its continued opposition to compulsory generic prescribing regardless of the status of the patient; and be it further

Resolved: That the intent of this Resolution be presented to the House of Delegates of the American Medical Association by delegates from the California Medical Association.

ACTION: *Adopted.*

Referred to: AMA Delegation.

1 1 1

VEXATIOUS LITIGATION

Resolution No. 92-67

Committee 3B

Introduced by: Los Angeles County Medical Association

WHEREAS, there is a steady yearly increase in both malpractice insurance rates and claims filed for malpractice; and

WHEREAS, many insurance underwriters are no longer willing to operate in all sections of California; and

WHEREAS, the California Bar Association has in the past recommended legislation aimed at cor-

recting the abuse of "Vexatious Litigation"; and

WHEREAS, "Vexatious Litigation" is widely associated with the increase in unjustifiable claims; now, therefore, be it

Resolved: That the California Medical Association Council, through its Liaison Committee to the State Bar Association, cooperate, and if possible form a joint recommendation aimed at legislative changes to correct the abuse of "Vexatious Litigation," such a joint resolution to be referred to the California Medical Association Council for approval.

ACTION: *Adopted.*

Referred to: Liaison Committee with State Bar of California.

1 1 1

CALIFORNIA PHYSICIANS' SERVICE COMMENDATION

Resolution No. 93-67

California Blue Shield Committee

Introduced by: Bernard Axelrod, M.D.

Representing: Los Angeles County Medical Association

WHEREAS, the California Physicians' Service has made a considerable and conscientious effort to solicit the cooperation and participation of the medical profession in the implementation of the Medi-Cal program; and

WHEREAS, despite the enormity of the task, it has with skill, diligence, and initiative, achieved a remarkable degree of success in discharging its responsibilities; now, therefore, be it

Resolved: That the California Medical Association commends California Physicians' Service for its accomplishments in implementing the Medi-Cal program.

ACTION: *Adopted.*

1 1 1

PUBLIC HEALTH LEAGUE

Resolution No. 94-67

Committee 3B

Introduced by: San Francisco Delegation

WHEREAS, it is imperative that the medical profession continue to support legislation favorable to good medical practice and oppose legislation that will be harmful to good medical practice; and

WHEREAS, the medical profession must continue to protect the public against poor medical practice often dependent upon and sometimes unwittingly promoted by legislation; and

WHEREAS, in order to carry on these objectives successfully the Public Health League, a non-partisan organization, organized and sponsored by the medical profession and allied professions of healing arts is our most effective legislative spokesman; and

WHEREAS, the Public Health League must have full support of membership to be fully effective; now, therefore, be it

Resolved: That the CMA ask each component society to stress that membership in the Public Health League is desirable and to make every effort to increase membership.

ACTION: *Adopted as amended.*

Referred to: Commission on Communications.

1 1 1

ROLE OF MEDICINE IN SOCIETY

Resolution No. 95-67

Committee 3

Introduced by: San Francisco Delegation

WHEREAS, four timely and pertinent statements and the accompanying recommendations have been prepared and approved by the CMA Committee on The Role of Medicine in Society during the past year; now, therefore, be it

Resolved: That these statements, known as the "Third Progress Report of the Committee on The Role of Medicine in Society" be made available only to CMA members and component medical societies for their evaluation for a period of 60 days and to other interested parties thereafter.

ACTION: *Adopted as amended.*

Referred to: Commission on Communications.

1 1 1

LABORATORY NOTIFICATION

Resolution No. 96-67

Committee 3B

Introduced by: San Francisco Delegation

WHEREAS, there is increased use of automated laboratories located in California and out-of-state; and

WHEREAS, a potential problem of notification by laboratories to the local health officer of diagnostically positive procedures for syphilis arises because of laboratories' geographical location; now, therefore, be it

Resolved: That the AMA investigate this problem nationally and arrive at appropriate recommendations.

ACTION: *Adopted as amended.*

Referred to: AMA Delegation.

1 1 1

COMMUNICABLE DISEASE REPORTING

Resolution No. 97-67

Committee 3B

Introduced by: San Francisco Delegation

WHEREAS, Section 3125 of the Health and Safety Code of the State of California requires physicians to report to the local health officer communicable disease; and

WHEREAS, Section 3125 lists fifty such diseases, many of which are no longer of major public health importance; and

WHEREAS, reporting of so many communicable diseases by physicians to the local health department is tedious, incomplete and of limited public health value; now, therefore, be it

Resolved: That the CMA, in conjunction with the State Department of Public Health seek changes in reportable disease, confining such diseases to those for which local health departments are prepared to engage in meaningful activities of epidemiologic control.

ACTION: *Adopted.*

Referred to: Commission on Public Agencies.

1 1 1

STATE LICENSING OF CLINICAL LABORATORIES

Resolution No. 98-67

Committee 3A

Introduced by: San Francisco Delegation

ACTION: *See resolution No. 62-67 with which this resolution was combined.*

1 1 1

CPS BY-LAW AMENDMENT

REMOVAL FROM OFFICE, CHAPTER III, SECTION 6

Resolution No. 99-67

California Blue Shield Committee

Introduced by: Richard S. Wilbur, M.D.

Representing: Council on Behalf of CPS-Blue Shield Board of Trustees.

Resolved: That Chapter III, Section 6, entitled "Removal from Office," of the by-laws of California Physicians' Service, be and the same hereby is amended by adding to said section the following: "A trustee who is absent from three consecutive regular meetings of the Board, without cause, shall automatically forfeit his office of trustee. 'Cause' includes illness, absence from the state, and other grounds acceptable to the Chairman of the Board." So that said Section 6 as amended will read:

"Any trustee may be removed from office as such by the affirmative vote of three fourths of the Administrative Members at any regular or special meeting of Administrative Members on written notice, setting forth the reasons and grounds therefor, mailed to such trustee at his last known address at least ten days prior to the date of such meetings. A trustee who is absent from three consecutive regular meetings of the Board, without cause, shall automatically forfeit his office of trustee. 'Cause' includes illness, absence from the state, and other grounds acceptable to the Chairman of the Board."

ACTION: *Adopted.*

Referred to: CPS-Blue Shield Board of Trustees.

CALIFORNIA BLUE SHIELD COMMENDATION
Resolution No. 100-67

California Blue Shield Committee

Introduced by: Glenn A. Pope, M.D.

Representing: Tenth District

Resolved: That the administration of California Blue Shield be commended for its recent establishment of a department devoted to labor and management health plan needs and that such department be encouraged to establish and maintain close liaison with the officers, governing bodies and staff of each component society of the California Medical Association.

ACTION: Adopted.

1 1 1

PHYSICIAN OPERATED LABORATORIES

Resolution No. 101-67

Committee 3A

Introduced by: Roger C. Isenhour, M.D.

ACTION: See resolution No. 62-67 with which this resolution was combined.

1 1 1

WEIGHT REDUCTION

Resolution No. 102-67

Committee 3B

Introduced by: Los Angeles County Medical Association Council

Resolved: That the following Statement of Policy concerning the physician's practice of weight reduction be adopted by the California Medical Association:

The practice of physicians concerned with weight reduction is a field of increased medical interest.

This field of practice is not a recognized specialty, but there is no ethical or legal ruling which would prevent a physician from limiting his practice to the treatment of obesity.

Any physician doing so, however, should recognize that his practice and the care of patients should follow all professional and ethical rules governing the practice of medicine. A physician should not advertise his services; he should not exploit the patient in any way. The use of drugs must be carefully controlled. Unproved or drugs in dangerous doses are never indicated.

The treatment of obesity requires very definite diagnostic skills and close supervision of the patient. It is vitally important that physicians working in this area have a thorough knowledge of all aspects of internal medicine. The methods which a physician uses must have a scientific basis and must not be based on dogma, cultism, or quackery, and be it further

Resolved: That the CMA Delegation introduce

this statement of policy regarding weight reduction to the AMA House of Delegates.

ACTION: Above substitute resolution adopted as amended and referred to Council.

Referred to: AMA Delegation.

1 1 1

GEORGE C. GRIFFITH, M.D.

Resolution No. 103-67

Committee 3B

Introduced by: Los Angeles County Medical Association Council

WHEREAS, George C. Griffith, M.D., is and has been an outstanding clinician in the private practice of medicine for forty-one years; and

WHEREAS, George C. Griffith, M.D., is and has been a medical scientist, investigator and educator throughout his entire professional life, which has earned him the affection and respect of his colleagues and many students; and

WHEREAS, George C. Griffith, M.D., has been a member of the Los Angeles County Medical Association for twenty-one years; and

WHEREAS, George C. Griffith, M.D., has been awarded the 1967 Gifted Teacher Award by the American College of Cardiology; and

WHEREAS, This is only the third such award ever presented by the College; and

WHEREAS, This award was presented by Doctor C. Walton Lillehei in the presence of the Vice President of the United States; now, therefore, be it

Resolved: That the California Medical Association takes this occasion to commend George C. Griffith, M.D., upon his receipt of the 1967 Gifted Teacher Award; and be it further

Resolved: That the California Medical Association express its appreciation to George C. Griffith, M.D., for his many years of exemplary service to the profession and to the public as a scientist and teacher, but most of all as a physician who personifies the most hallowed traditions of the medical profession.

ACTION: Adopted as amended.

Referred to: Commission on Communications.

1 1 1

VIRUS LABORATORY SERVICES

Resolution No. 104-67

Committee 3B

Introduced by: San Francisco Delegation

WHEREAS, viral infections, caused by over 150 different virus types, are responsible for hundreds of thousands of illnesses and hundreds of deaths in California each year; and

WHEREAS, certain viral infections during pregnancy, particularly rubella, cause serious defects or deformities of the infant; and

WHEREAS, laboratory diagnostic tests not previously available have recently been developed for many viral infections, including rubella and common respiratory infections; and

WHEREAS, laboratory tests are essential to assist physicians in the definitive diagnosis of viral infections; and

WHEREAS, the Virus Laboratory of the State of California Department of Public Health provides the sole source of such services; now, therefore, be it

Resolved: That the Virus Laboratory of the State of California Department of Public Health be complimented for its work, particularly in testing for rubella virus and antibodies, and be encouraged to continue and expand the service, lending assistance to local public and private facilities dealing with viral infections.

ACTION: *Adopted.*

Referred to: Commission on Public Agencies.

1 1 1

COMPREHENSIVE HEALTH PLANNING

Resolution No. 105-67 **Committee 3**

Introduced by: San Francisco Delegation

WHEREAS, Public Law 89-749 provides for comprehensive health planning for services, manpower and facilities at the state, regional and local level; and

WHEREAS, these planning efforts (voluntary and/or governmental) will be coordinated and developed in directions far greater than those which exist at present; and

WHEREAS, this will involve new concepts and activities that require wide and objective representation in all planning groups working in concert with the health professions; now, therefore, be it

Resolved: That the CMA become involved in comprehensive health planning and offer its services to the State Department of Public Health and make recommendations concerning proper methods of carrying out this responsibility to the citizens of California; and be it further

Resolved: That the CMA urge each component medical society to offer its services and technical skills to its regional and local comprehensive health planning groups.

ACTION: *Adopted as amended.*

Referred to: Commission on Public Agencies and Commission on Community Health Services.

BILLING FOR ANESTHESIA

Resolution No. 106-67 **Committee 3A**

Introduced by: San Francisco Delegation

ACTION: *No action was taken on this resolution.*

1 1 1

EMERGENCY CARE

Resolution No. 107-67 **Committee 3**

Introduced by: Glenn A. Pope, M.D.

Representing: Tenth District

ACTION: *Not adopted.*

1 1 1

LEGISLATION-INFLUENCED CHANGE IN THE PRACTICE OF MEDICINE

Resolution No. 108-67 **Committee 3A**

Introduced by: Mason Hohl, M.D.

Representing: Los Angeles County Medical Association

WHEREAS, the elected representatives of the people of the United States, after due consideration, have passed far reaching Legislation affecting the practice of medicine; and

WHEREAS, the implementation of Public Law 89-97, and of various comparable State Programs, has in fact changed the practice of medicine; and

WHEREAS, these changes affect the types of care that can be rendered both in and out of hospitals, largely influenced by the shortage of hospital beds; and

WHEREAS, it is no longer possible in many localities to obtain hospital beds for other than emergencies; and

WHEREAS, patients are asking constantly, "How did this come about?"; now, therefore, be it

Resolved: That the California Medical Association and its officers engage in a Statewide educational campaign directed to the people, informing them as to the effects that this legislation has had upon the practice of medicine and how it will affect them in times of illness; and be it further

Resolved: That this resolution be taken by the California Delegation to the American Medical Association for similar consideration for a nationwide educational program.

ACTION: *Referred to Council.*

Referred to: Commission on Hospital Affairs, Commission on Communications and AMA Delegation.

AMENDMENTS TO CONSTITUTION AND BYLAWS

Amendments to the Constitution and Bylaws may be introduced at any session of the House of Delegates. Amendments to the Bylaws may be acted upon 24 hours after introduction, while amendments to the Constitution must lie on the table until the next regular meeting of the House of Delegates.

Reference Committee No. 4 considers all proposed amendments to both the Constitution and the Bylaws. Under the required waiting periods, all Constitutional amendments introduced in 1966 were brought before the House of Delegates for action in 1967. In some instances, proposed amendments to the Bylaws are also held over for one year, where they are entered as companions to proposed amendments to the Constitution.

ACTIONS

Listed below are actions taken by the House of Delegates on all proposed amendments to the Constitution and Bylaws presented for action this year. A two-thirds affirmative vote is required for passage of all amendments. New language approved is shown in italics.

1966

CONSTITUTIONAL AMENDMENTS ACTED UPON IN 1967

Six constitutional amendments were introduced in the 1966 House of Delegates and, under the terms of the Constitution, must lie on the table until the next regular meeting of the House of Delegates.

These proposed Constitutional amendments were printed in two issues of CALIFORNIA MEDICINE before they came before the House of Delegates for action.

CONSTITUTIONAL AMENDMENT NO. 1-66

PHYSICIANS' BENEVOLENCE FUND

Introduced by: Council

ACTION: *Not adopted.*

1 1 1

CONSTITUTIONAL AMENDMENT NO. 2-66

COMPOSITION OF THE COUNCIL

Introduced by: Council

Resolved: That Article III, Part B, Section 9, of the California Medical Association Constitution, be deleted and the following amendment be adopted:

"The Council shall consist of:

"(a) Elected councilors from the councilor districts set forth in Section 10. Each councilor district shall be entitled to elect one (1) councilor for each 1,000 active members, or major fraction thereof, according to its membership as of the first day of September of the preceding year; provided, that each councilor district shall be entitled to a minimum of one (1) councilor.

"(b) Elected councilors from any one district shall not, at any time, exceed 40 per cent of the total Council membership.

"(c) The president, president-elect, immediate past president, speaker and vice-speaker.

"(d) The secretary and editor, when they are members of the Association, and one member of the Executive Committee of the Scientific Board who shall be elected by the Executive Committee of that body from representatives of the scientific sections or members-at-large. These three persons shall be ex officio members of the Council without the right to vote."

ACTION: *Adopted.*

1 1 1

CONSTITUTIONAL AMENDMENT NO. 3-66

OFFICERS

Introduced by: Council

Resolved: That Article VI, Section 1, of the Constitution of the California Medical Association be amended by adding the language in italics and deleting the language shown in parentheses so that it shall read:

"Section 1.—Officers

"The officers of this Association shall be a President, a President-Elect, (a Secretary) a Chairman of the Council, a Vice-Chairman of the Council, a Speaker of the House of Delegates, a Vice-Speaker of the House of Delegates and, when they are members of the Association, a Secretary and an Editor."

ACTION: *Adopted.*

1 1 1

CONSTITUTIONAL AMENDMENT NO. 4-66

CONSTITUTIONAL AMENDMENT TRANSFERRING AMADOR COUNTY TO FIFTH DISTRICT

Introduced by: Tenth District

WHEREAS, Article III, Part B, Section 10 of current CMA Bylaws places Amador County in Councilor District Number Ten; and

WHEREAS, only two of the 12 medical doctors licensed in Amador County maintain county society affiliation in a Tenth District society, the majority, because of travel patterns and hospital locations, preferring to affiliate with a county medical society in the Fifth District; and

WHEREAS, the Fifth and Tenth District delegations have endorsed such transfer of Amador County to the Fifth District; now, therefore, be it

Resolved: That Article III, Part B, Section 10 of the Constitution of the CMA be amended by adding the words in italics and deleting the words in parentheses, and to read:

"District Number Five, comprising *Amador*, Kern, Kings, Tulare, Fresno, Madera, Mariposa, Merced, Stanislaus, San Joaquin, Calaveras and Tuolumne Counties.

"District Number Ten, comprising Sacramento, (Amador,) Alpine, El Dorado, Placer, Nevada, Sierra, Yuba, Sutter, Yolo, Colusa, Glenn, Butte, Plumas, Tehama, Trinity, Shasta, Lassen, Modoc, and Siskiyou Counties."

ACTION: Adopted.

CONSTITUTIONAL AMENDMENT NO. 5-66

ESTABLISHING A SEPARATE COUNCILOR DISTRICT FOR THE COUNTY OF ORANGE

Introduced by: Orange County Medical Association

Resolved: That Article III, Part B, Section 10, Councilor District of the CMA Constitution be deleted and the following Section 10 substituted therefor.

"There are 12 districts as follows:

"District Number One, comprising San Diego.

"District Number Two, comprising Imperial, Riverside, San Bernardino, Mono and Inyo Counties.

"District Number Three, comprising Orange County.

"District Number Four, comprising the County of Los Angeles.

"District Number Five, comprising Ventura, Santa Barbara and San Luis Obispo Counties.

"District Number Six, comprising Kern, Kings, Tulare, Fresno, Madera, Mariposa, Merced, Stanislaus, San Joaquin, Calaveras and Tuolumne Counties.

"District Number Seven, comprising Monterey, San Benito, Santa Cruz, Santa Clara and San Mateo Counties.

"District Number Eight, comprising San Francisco County.

"District Number Nine, comprising Alameda County and Contra Costa County.

"District Number Ten, comprising Marin, Solano, Napa, Sonoma, Lake, Mendocino, Humboldt and Del Norte Counties.

"District Number Eleven, comprising Sacramento, Amador, Alpine, El Dorado, Placer, Nevada, Sierra, Yuba, Sutter, Yolo, Colusa, Glenn, Butte, Plumas, Tehama, Trinity, Shasta, Lassen, Modoc and Siskiyou Counties.

"District Number Twelve, consisting of any society which is not limited as to geographical area, or the area of which overlaps the area covered by one or more existing component societies; such society and its members shall not be considered to be members of any other councilor district."

ACTION: Adopted.

CONSTITUTIONAL AMENDMENT NO. 6-66

REVISION OF DISTRICT ONE

Representing: Imperial

Introduced by: Burke E. Schoensee

Resolved: That Article III, Part B, Section 10 of the Constitution be amended by revising District Number One to include San Diego and Imperial Counties, and that Imperial County be deleted from District Number Two, and that otherwise said Section remain unaltered.

ACTION: Adopted.

BYLAW AMENDMENTS

TERMINATION, SUSPENSION OR PROBATION OF MEMBERSHIP; CHAPTER II, SECTION 10(c)

Bylaws No. 1-67

Committee 4

Introduced by: Council

Resolved: That Chapter II, Section 10(c) of the Bylaws of the California Medical Association be amended by deleting the language in parentheses and inserting the language in italics, so that the section shall read:

"(c) By Revocation, Suspension or Probation of Physician and Surgeon's Certificate. (Any member whose license to practice medicine and surgery in the State of California is revoked or suspended shall, upon receipt of written evidence of such revocation or suspension by the secretary of this Association, thereupon cease to be a member of this Association.)

"The governing body of a component society, upon receipt of a copy of the State Board of Medical Examiners' notice of revocation or suspension of license to practice medicine, shall take formal action to terminate or suspend membership.

"The governing body of a component society, upon receipt of a copy of the State Board of Med-

ical Examiners' notice that a member of the component society has been found guilty of a disciplinary charge and has been placed on probation for a stated period of time, may take formal action to cause the member to be placed on probation for a concurrent period of time."

"(Receipt of written evidence that the Board of Medical Examiners has found a member guilty of a disciplinary charge but has suspended judgment and placed him on probation for a stated length of time, shall thereupon cause the member to be a probationary member of the Association for a concurrent period of time.)"

ACTION: Adopted as amended.

1 1 1

DUTIES OF DISTRICT COUNCILORS; CHAPTER VI, SECTION 8

Bylaws No. 2-67

Committee 4

Introduced by: Council

Resolved: That Chapter VI, Section 8 of the Bylaws of the California Medical Association be amended by deleting the words in parentheses so that the section shall read:

"Section 8.—Duties of District Councilors

"Each district councilor shall be organizer, peacemaker and censor for his district. He shall visit each county in his district at least once a year for the purpose of organizing component societies where none exist, of inquiring into the condition of the profession, and of maintaining touch with the activities of the component societies (of) *in* his district. He shall (in writing) make an annual report of his work and of the condition of the profession (of) *in* each county in his district to the Council, which shall take such action thereon as it may deem best."

ACTION: Adopted.

1 1 1

APPOINTMENT OF SECRETARY, EXECUTIVE DIRECTOR, ASSISTANT SECRETARIES, EDITOR AND ASSOCIATE EDITOR;

CHAPTER VI, SECTION 12; CHAPTER VI, SECTION 14—CHAPTER IX, SECTION 2

Bylaws No. 3-67

Committee 4

Introduced by: Council

Resolved: That Chapter VI, Section 12 of the Bylaws of the California Medical Association be amended by inserting the words "an executive director" after the word "secretary" so that Section 12 shall read:

"The Council shall (employ) *appoint* a secretary, *an executive director* and an editor, and, in its discretion, one or more assistant secretaries or

associate editors. The terms of their (employment) *appointment* shall be such as are satisfactory to the Council(,). (provided, however, that) *When the appointment requires employment*, no contract (of employment) shall, by its terms, exceed a period of three (3) years from the date or the organization meeting at which such contract is authorized."; and be it further

Resolved: That Section 14 of Chapter VI of the Bylaws is hereby repealed; and be it further

Resolved: That Section 2 of Chapter IX of the Bylaws is hereby amended by substituting the words "executive director" for the words "executive secretary" in the heading of said section and in the first paragraph of the section.

ACTION: Adopted as amended.

1 1 1

COMMITTEE ON ADVERSE DRUG REACTIONS CHAPTER VI, SECTION 2(i)

Bylaws No. 4-67

Committee 4

Introduced by: Council

Resolved: That Chapter IV, Section 2(i) be amended to change the name of the Committee on Dangerous Drugs and Adverse Drug Reactions. The deletions are shown in parentheses and the new sections are in italics, as follows:

"(i) (Committee on Dangerous Drugs and Adverse Drug Reactions.) *Committee on Drugs.* (The Committee on Dangerous Drugs and Adverse Drug Reactions) *The Committee on Drugs* shall study the medical problems relating to narcotics and dangerous and hypnotic drugs and the adverse reactions from drugs."

ACTION: Adopted as amended.

1 1 1

COMMITTEE ON VETERANS AFFAIRS

Chapter VII, Section (a)

Bylaws No. 5-67

Committee 4

Introduced by: Council

Resolved: That a new subsection (a)(5) be added to Chapter VII, to make a new Committee on Veterans Affairs under the Commission on Medical Services, so that the committees would be: (The new section is shown in italics.)

- "1. Committee on Fees,
- "2. Committee on Federal Medical Care Programs,
- "3. Committee on Mediation,
- "4. Committee on Insurance and Prepayment,
- "5. *Committee on Veterans Affairs.*"

ACTION: Adopted.

COMMITTEE ON MEDICAL ASPECTS OF SPORTS
& PHYSICAL FITNESS—CHAP. VII, SEC. 1(c) (6)

Bylaws No. 6-67

Committee 4

Introduced by: Council

Resolved: That Chapter VII, Section 1(c) (6) shall be amended by adding the words in italics, as follows:

“6. Committee on Medical Aspects of Sports and Physical Fitness.”

ACTION: Adopted.

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REFERENDUM PETITIONS, CHAP. XII,
SECS. 5 AND 6

Bylaws No. 7-67

Committee 4

Introduced by: Council

Resolved: That the present Section 5 of Chapter XII of the Bylaws of the California Medical Association be deleted and the following section be adopted in its stead, and that Section 6 be added:

“Section 5.—Referendum Petitions

“(a) The proponents of any proposed member referendum measure, prior to the circulating of any petition for signatures thereon, shall submit a draft of the petition to the legal counsel of the California Medical Association, with a request that he prepare a summary of the chief purposes and points of the proposed measure in less than one hundred words. The legal counsel shall also provide a title for the referendum petition. The title and summary shall be returned to the proponents within ninety (90) days.

“(b) The proponents of any proposed referendum shall place the following information at the top of each page whereon signatures are to appear: ‘Referendum Petition—California Medical Association,’ including a title and summary.

“(c) Each line of the petition shall provide one column for the written signature of an active member of the California Medical Association and another column for printing the active member’s name. The determination of a signer’s membership shall be made by the California Medical Association legal counsel.

“(d) A valid referendum petition shall require 250 signatures. Included among the total of 250 signatures shall be at least twenty-five (25) each from four (4) councilor districts.

“Section 6.—The Election

“(a) Upon receipt of the proper number of referendum petition signatures, it shall be the responsibility of the California Medical Association Council to arrange for the collection and printing of one article for and one article against

the proposed referendum. Articles shall be limited to one thousand words and shall be signed by not more than three members.

“(b) The referendum ballot, along with the referendum title, summary and arguments for and against the proposed referendum, shall be prepared by the California Medical Association legal counsel or by an independent organization chosen by the California Medical Association Council. Ballots shall be distributed to component medical societies in time for their use at the annual election of California Medical Association delegates and alternates.

“(c) After the annual elections in component societies, all referendum ballots shall be returned to the office of the secretary of the California Medical Association.

“(d) A majority of the votes cast by the active members voting shall cause the adoption of the referendum proposal, except that changes in the California Medical Association Constitution or Bylaws shall require a two-thirds affirmative vote of the votes cast.

“(e) A member referendum ballot may be conducted prior to the annual election of California Medical Association delegates and alternates, by direct mail ballot, upon the approval of a majority of the California Medical Association House of Delegates or a two-thirds vote of the California Medical Association Council, according to Chapter XII, Section 3, of the California Medical Association Bylaws.”

ACTION: Adopted.

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ADDRESSES AND SCIENTIFIC PAPERS,
CHAPTER IV, SECTION 6

Bylaws No. 8-67

Committee 4

Introduced by: Council

Resolved: That Chapter IV, Section 6, of the CMA Bylaws be amended by deleting the language in parentheses and adding the language in italics:

“The program at Annual Sessions shall be divided between general meetings and section meetings as the Council shall deem appropriate.

“At the general meetings, the president may deliver an address, and, with the sanction of the Council, other addresses and reports may be presented.

“Excepting the president’s address and such other addresses and reports as the Council may determine, no address or paper shall occupy more than twenty minutes in delivery.

“No member, except by unanimous consent, shall speak more than once in the discussion of

any paper nor longer than five minutes at any one time. This subsection of the Bylaws shall be printed on all programs of general and section meetings.

"(All papers read before this Association shall be its property. Each paper, when it has been read, shall be deposited with the secretary of the section, by him to be promptly turned over to the secretary of the Association.)

"(Authors of papers read before this Association shall not cause them to be published elsewhere except with the consent of the Editorial Board.)

"If a speaker wishes his paper to be considered for publication in CALIFORNIA MEDICINE, he shall immediately after reading it deposit it with the secretary of the section who shall promptly turn it over to the Editor of CALIFORNIA MEDICINE, or his representative."

ACTION: Adopted.

PAYMENT OF DUES, SECTION II, SECTION 10(b)

Bylaws No. 9-67

Committee 4

Introduced by: Council

ACTION: Not adopted.

COMMITTEE ON SCIENTIFIC INFORMATION, COMMITTEE ON CANCER EDUCATION, COMMITTEE ON TUMOR TISSUE REGISTRY, COMMITTEE ON CONSULTATIVE TUMOR BOARDS,

COMMITTEE ON CARDIOVASCULAR DISEASES;
CHAP. IV, SECTION 2(d), (e), (f), (g), (h), (i)

Bylaws No. 10-67

Committee 4

Introduced by: Council

Resolved: That Chapter IV, Section 2 of the California Medical Association Bylaws be amended by deleting subsection (d), the Committee on Scientific Information and subcommittees (1), (2) and (3) of subsection (f), Committee on Cancer Education, Committee on Tumor Tissue Registry and Committee on Consultative Tumor Boards, and increase from seven (7) to nine (9) the membership on the Committee on Cancer.

Subsection (e) should be redesignated subsection (d); subsection (f) should be redesignated subsection (e); subsection (g) should be redesignated subsection (f); subsection (h) should be redesignated subsection (g); subsection (i) should be redesignated subsection (h).

A new subsection (i) should be added as follows:

"(i) Committee on Cardiovascular Diseases.

"The Committee on Cardiovascular Diseases

shall consist of five (5) members, one of whom shall be from the Scientific Board. The committee shall be responsible for activities of this Association in the field of cardiovascular research and prevention, and control of cardiovascular disease and liaison with other state agencies active in cardiovascular disease control."

ACTION: Adopted as amended.

EXPENSES OF COUNCILORS AND OFFICERS, CHAPTER VI, SECTION 9

Bylaws No. 11-67

Committee 4

Introduced by: Council

Resolved: That Chapter VI, Section 9 of the Bylaws of the California Medical Association be amended by adding the italicized words, so that Section 9 shall read:

"Section 9.—Expenses of Councilors and Officers.

"Councilors and officers shall be allowed railroad, *air* fare or mileage, plus an allowance for maintenance expense, (a) in attending Association, district or county society meetings, (b) meetings of committees of the Association; (c) authorized councilor or officer visits to county societies; (d) and otherwise when on official business, authorized or approved by the Council."

ACTION: Adopted.

FOR ACTION IN 1968

One constitutional amendment was introduced in the 1967 House of Delegates and, under the terms of the Constitution, must lie on the table until the next regular meeting of the House of Delegates.

This proposed amendment is shown here for the information of the membership. In addition, the proposed Constitutional amendment is required to be printed in two issues of CALIFORNIA MEDICINE before it comes before the House of Delegates for action.

CONSTITUTIONAL AMENDMENT NO. 1-67

Woman's Auxiliary; Article I, Sec. 6

Introduced by: Council

Resolved: That a new Section 6 be added to Article I, as follows:

"Section 6.—Woman's Auxiliary to the California Medical Association.

"In addition to the organizational structure previously set forth in this Article, this Association may charter a Woman's Auxiliary to the California Medical Association, and components

thereto, which shall be considered an integral part of the Association but which shall conduct its own organization and business separate and distinct from the Association and its Societies, subject to the following requirements:

"a. The name of the Auxiliary shall be 'Woman's Auxiliary to the California Medical Association,' (hereinafter referred to as Auxiliary);

"b. The purpose of the Auxiliary shall be to promote the science and art of medicine, the protection of public health and the betterment of the medical profession, and to promote similar interests of its component Auxiliaries;

"c. The Auxiliary shall be composed of the component Auxiliaries and their members;

"d. Component Auxiliaries shall include all women's auxiliaries to component Medical Societies of the California Medical Association heretofore or hereafter chartered by this Association;

"e. Charters to component Auxiliaries shall be granted and revoked by the Association as it may provide; provided that no charter issued by the Association, nor any action of the Association in issuing or revoking such charters, shall conflict with the purposes and principles of this Association as set forth in its Constitution and Bylaws."



Council Meeting Minutes

531st Meeting

Tentative Draft: Minutes of the 531st Meeting of the Council, Los Angeles, April 14 to 19, 1967.

The meeting was called to order by Chairman Anderson in the headquarters of the Los Angeles County Medical Association, on Friday, 14 April at 4:00 p.m. and thereafter was recessed and reconvened in the Biltmore Hotel on each of the succeeding days through 19 April 1967.

A quorum was present and acting (full roll call, including names of invited guests, appears in item 36).

1. Minutes for Approval

The minutes of the 529th meeting of the Council, held 25 February 1967 were approved as distributed.

The minutes of the 530th meeting of the Council, held 21 March 1967, were approved as amended.

2. 1967 Annual Session

Chairman Anderson asked that each Councilor select a reference committee for which he would be responsible. Chairman Anderson brought before the Council three late resolutions for consideration on an emergency basis. None received approval for submission to the House of Delegates.

Doctor Anderson asked Council approval for the "Statement of CMA Goals" to be submitted to the House of Delegates as a supplemental report to the Council.

ACTION: Voted to approve the statement and to submit it to the House of Delegates.

3. Finance Committee

On behalf of the Finance Committee, Doctor Kay recommended that the CMA pension plan for employees be modified to provide vested interest for persons who have been employed 10 years and have reached age 40.

ACTION: Voted to approve the addition of vested interest to the CMA Employee Pension Plan.

A study of the current pension and life insurance plans for CMA employees was recommended. Doctor Kay said that such a study would involve evaluation of the feasibility of expanding the coverages and bringing them into line with comparable plans.

ACTION: Voted to approve a study of the current pension and life insurance plans for CMA employees.

Doctor Kay recommended that CMA decline a request for a contribution towards rebuilding St. Mary's Church in San Francisco.

ACTION: Voted to decline the request.

The "health education" function was discussed and the Finance Committee recommended that CMA activity in this area be expanded and included as a budgeted item in the 1967-68 budget with a maximum expenditure of \$25,000 allocated for this purpose. The funds would fall under the classification of Commissions and Committees.

ACTION: Voted to expand CMA's "Health Education" function (\$25,000 to be included in the 1967-68 budget for this purpose).

The financing of a one-day meeting with specialty societies was considered. The Committee recommended that a maximum of \$1,500 be contributed by CMA (to cover meals and meeting rooms).

ACTION: Voted to approve the allocation of \$1,500 to help pay the costs of a one-day conference with specialty societies.

4. Committee on Appeals

A written report for the information of the Council was submitted by Chairman Pheasant. The report outlined the purpose of the Committee, its areas of responsibility, its makeup and operating format. The report stated that, acting on behalf of and through the Commission on Medical Services, the Appeals Committee should act as the professional review body of the Association in relation to questions, grievances or appeals from patients, physicians, county medical societies and carriers in the application of provisions of P.L. 89-97 and Medi-Cal.

5. Commission on Community Health Services

Chairman Kay asked Council approval for the CMA Committee on Traffic Safety to evaluate applicants' medical information for the Department of Motor Vehicles.

ACTION: *Voted to approve such action by the Committee on Traffic Safety.*

6. *Ad Hoc Committee on LACMA Library*

Doctor Kay reported that the ad hoc Committee had met and that it had recommended a \$5,000 allocation for the LACMA library be made in all ensuing CMA budgets. The committee also recommended that it not be made a standing library committee.

ACTION: *Voted an Annual allocation of \$5,000 to the LACMA Library.*

ACTION: *Voted to maintain the Committee on an ad hoc basis.*

7. *Preview of CMA's Subsidiary Organizations*

Executive Director Howard Hassard outlined for the Council the financial structure of the CMA, including brief descriptions of its subsidiary and affiliated organizations.

Included as subsidiary organizations are: Trustees of the California Medical Association, an incorporated nonprofit company whose sole purpose is to hold excess funds contributed by the Association as a result of its operating at a lesser cost than its receipts; Physicians' Benevolence Fund, Inc., a corporation maintained to provide benevolences to needy physicians or their families, which can receive gifts and bequests from members of the Association; Six Ninety Three Sutter Publications, Inc., a corporation to distribute CMA publications for which there is a charge; California Medical Education and Research Foundation, a nonprofit corporation maintained to carry on research activities in the field of medical economics and which is tax-exempt and qualified to receive contributions on a tax-deductible basis for the donor; and Audio Digest Foundation, a corporation which produces and sells tape recordings of medical papers or digest of papers in medical publications, with CMA being the sole stockholder. Mr. Hassard pointed out that the Councilors of CMA, by virtue of being Councilors, are members of or make up all of the affiliated organizations of CMA. All but the Audio Digest Foundation have their annual meetings in conjunction with the CMA Annual Session.

8. *Preliminary Report of the Planning and Goals Conference on Continuing Medical Education*

Doctor Donald Petit, chairman of the CMA Committee on Continuing Medical Education, re-

ported to the Council on the Planning and Goals Conference held 10 to 12 March in San Diego, to discuss problems of major importance in continuing medical education in California. The program, he related, was divided into four sections: Relationship and role of community hospital staffs and university medical centers; Evaluation of post-graduate and continuing medical education; Motivation for doctors to participate in continuing medical education; and Mechanisms for certifying or accrediting continuing medical education courses. Doctor Petit reviewed some of the recommendations emanating from the conference sections, and asked for Council approval of the report. Discussion of various recommendations followed.

ACTION: *Voted to approve the preliminary report in principle and refer back to the Scientific Board for further study and implementation.*

9. *Commission on Medical Services*

Speaking for the Commission, Chairman Howard reported that as of 1 July 1967 the Military Dependents' Medical Care Program (CHAMPUS) will be on a usual, customary and reasonable basis for reimbursement. California Blue Shield, the fiscal intermediary, will assume certain responsibilities under this program such as providing to CHAMPUS quarterly reports regarding physicians' fees, average charges and physician profiles.

10. *Status Report on Research Activities*

A written report was submitted for the Council's information, reviewing the progress of various research activities in which the Bureau of Research and Planning is presently engaged or may be contemplating. Chairman Sherman gave no further report.

11. *Commission on Communications*

Chairman Todd spoke to the Council about the report, "Strengthening Health Care for Californians," distributed earlier in the Council meeting. He stated that the report was prepared by the Commission for distribution to opinion leaders in California to present the CMA story of activities and involvement in a wide variety of areas relating to health care.

12. *Utilization Review in Extended Care Facilities* (Commission on Public Agencies)

Councilor Kaiser, chairman of the CMA Subcommittee on Utilization Review for Extended

Care Facilities, presented to the Council for its information a report prepared by the subcommittee. He said that the subcommittee had labored over definitions in this very involved area, and these were included in the report. The report pointed out that, by a recent directive from the State Health and Welfare Agency, county medical consultants were placed in a key position regarding admission and utilization by convalescent hospitals, and CMA recommended close cooperation with these persons by the local committees. The report also asked for questions and suggestions to be sent to the subcommittee to stimulate two-way communication.

13. *Practice of Unlicensed Physicians in County and Teaching Hospitals*

Doctor Irving Schor, President of the Tulare County Medical Society, reported to the Council on SB 1422, a proposed amendment of the California Business and Professions Code introduced by Senator Howard Way, to allow physicians licensed in a state other than California to practice as staff physicians in county and teaching hospitals for a period of one year. Council approval was sought and discussion followed.

ACTION: *Voted not to support SB 1422.*

14. *Committee on Organizational Review And Planning*

Chairman Teall outlined the progress of the committee at its four meetings and made several recommendations to the Council. The Committee urged the Council to create a task force to conduct studies on physician manpower needs in California.

ACTION: *Voted to table the creation of such a task force until progress from the Health Manpower Council can be evaluated.*

The Committee also recommended that the Council stimulate all appropriate committees to give high priority to establishing liaison with allied health care groups and to exploring the proper relationships between allied health care persons and physicians at the present time and for the future.

ACTION: *Voted approval of the concept.*

Doctor Teall also proposed to the Council that the ad hoc Committee to Study Relations of CMA with Component Medical Societies be made a per-

manent subcommittee to the Committee on Organizational Review and Planning, with its primary purpose of continuing review of staff organizational structure and needs.

ACTION: *Voted to table the motion.*

Doctor Teall stated that it was the opinion of the Committee that it should be continued for the coming year on an ad hoc study committee basis (maintaining its present format) and asked Council approval of this recommendation.

ACTION: *Voted to approve the continuation of the Committee on Organizational Review and Planning on an ad hoc study committee basis for the ensuing year.*

15. *California Blue Shield*

Doctor Richard Wilbur, chairman of the Blue Shield Board, reported to the Council that, since 1 January, 12,000 new standard program Blue Shield members and 8,000 CPIC members have been added.

The Blue Shield high option federal employees program, Doctor Wilbur stated, is to go on the usual and customary fee 1 July 1967, which will involve 258,000 persons. He said that Blue Shield is making every effort to sell the usual and customary fee program to new business and to the existing business through persuasion and through voluntary conversion. Blue Shield now has 444,000 persons either already under usual and customary programs or who are committed to such plans within the next few months.

Doctor Wilbur stated that Blue Shield reported to the Assembly Public Health Committee that its combined Blue Shield-Blue Cross administrative expense for handling the Medi-Cal program the first year was 1.54 per cent. Blue Shield has now processed 14 million claims and has paid out \$173 million under Medi-Cal. Under Medicare, he reported, Blue Shield has processed about 1½ million claims and paid out \$41 million. Blue Shield is currently receiving about 65,000 Medicare claims per week and in the last month processed 200,000 more Medicare claims than had been received.

The Blue Shield bylaws, Doctor Wilbur informed the Council, were revised to limit lay trustees as well as physician trustees to two consecutive terms, so that all elected trustees will be treated the same. Blue Shield simultaneously voted to recommend to the Council that the CMA Coun-

cil appointees be similarly restricted and that after an appointee has served six consecutive years, that he not be reappointed to the Blue Shield Board for at least one year. This would mean, he explained, that all trustees on the Board would be subject to the same limitations.

16. *Reports of Medical School Deans*

Dean Egeberg of the University of Southern California School of Medicine reported that the school had had a site visit from persons in Washington for consideration of USC as a Heart Disease, Cancer and Stroke center. He said that they had no word as yet regarding the awarding of grants or sites, but the news would be forthcoming.

Dean Bostick of the University of California-California College of Medicine, said that a report had been made as far as a location for the California College of Medicine. He said that it was recommended that it be placed on the Irvine Campus in Orange County, as it seemed to have the most appropriate promise for medical growth and resources. The report was submitted to the Regents and was accepted unanimously. He said it then went to the Trustees, who acted in accord with the Regents. He said that it still must return to the Regents before becoming final.

Dean Tupper of the University of California Medical School at Davis reported that the school is moving ahead for its target of admitting 48 freshmen medical students in the fall of 1968. He also informed the Council that the Sacramento Society for Medical Improvement had established a grant in aid and scholarship program for medical students from Sacramento County, wherever they may be in medical school.

17. *State Department of Rehabilitation*

The new director, Mr. Robert Howard, was introduced to the Council by Dr. Richard Young, medical director of the State Department.

18. *State Department of Mental Hygiene*

Doctor James V. Lowry, director of the Department, reviewed for the Council current developments in the area of budgetary modifications. These main points emerged:

a. The new Administration decided to submit a budget covering "current programs" only, rather than one which would also cover "Improvements and new programs."

b. This budget calls for:

—reductions in the areas of headquarters expenditures in research and training and in *non-patient* care personnel. No reductions were proposed for patient care personnel in hospitals for the mentally retarded. The Governor has given his assurance that if non-patient care personnel reductions decrease the amount of time that other personnel can devote to patient care, those non-patient personnel would be reinstated.

—no reductions in the two children's facilities and the two facilities for adolescents at Napa and Camarillo.

—discontinuation of *only* those local services for the mentally ill and mentally retarded that can be incorporated within local mental health programs and funded under the Short-Doyle programs. (There was a \$4,000,000 *increase* in funds to support local programs. Many may receive 100 per cent financing from the State.)

c. The new budget reflects a 9 per cent reduction in costs of direct operations for the Department—from \$193.5 million to \$176.5 million.

d. More importantly, the budget calls for a 22 per cent increase in Short-Doyle funds—from \$19,350,000 to \$23,600,000.

e. The budget as a whole reflects a 5.9 per cent decrease—from \$212 million to \$200 million.

f. Quality of care *will not diminish* under the new budget, judging by two major criteria.

—*Number of dollars spent per patient* (this year, \$4,485 per patient year was spent; under the new budget, \$5,007 would be spent.

—*Ratio of staff to patient* (if patient population decrease estimates are accurate, the ratio will be the same on 30 June 1968 as it is now—about 2.34 to 1).

g. No delay in admissions will result from these budgetary changes (State mental facilities had 1,000 fewer admissions in the last fiscal year than the previous year).

Following consideration of Doctor Lowry's report, the following statement was offered as policy of the Association:

CMA continues to offer its advice and counsel to the state administration to promote medical excellence and a sound fiscal basis in the state's mental health programs.

This position represents a reaffirmation of previous policy adopted by the Council on 21 March 1967:

"The Council reaffirmed its previous position in regard to the CMA Study of State Hospitals. It urges economies of operation in all branches of the State Government. This, however, without interference with adequate patient care, or prevention of prompt discharge."

ACTION: *Voted to approve the above statement as CMA policy.*

19. *State Department of Public Health*

Doctor Lester Breslow reported that although many serious diseases had been virtually eliminated, the two that have risen to importance are tuberculosis and measles. He said that an effective measles vaccine is now available and that he hoped we would see a reduction in the incidence of measles in the coming year. He also noted that several county medical societies either had carried out a community-wide program of measles vaccination or had committed themselves to do so, and he hoped that others would follow. He reported that tuberculosis is receiving much study and it was hoped that its incidence would also be on the decline soon.

Doctor Breslow also reported that Social Security Administration had met recently and had created some new definitions regarding long-term care facilities, as they relate to certification qualifications. He said that he hoped California would continue licensing in the same manner as it has been doing, with adaptations to federal regulations only as necessary.

20. *Office of Health Care Services*

Doctor Rosen reported to the Council that the checks for the first group of cleared claims backlog, created by inability to establish eligibility, under the Medi-Cal program, were already in the mail and the others would be going out daily. He also stated that changes were being made in the system to expedite and simplify the problem of determining eligibility so that this type of backlog would not occur in the future.

21. *State Department of Employment*

Doctor Radl, director of the Department, thanked the Council and all the members of CMA who assisted the Department in the program for disability insurance and in setting up the Manpower Development Training Authority.

22. *Bureau of Health Insurance, Social Security Administration*

Mrs. Mercia Kahn, western regional director of the Bureau of Health Insurance, introduced to the Council Mr. Keith Olsen, a new member on her staff. She also reported that certification of extended care facilities had now reached 688, covering 50,017 beds. Hospital certification is now up to 504 and there are 97 home health care agencies certified. She also informed the Council that 458 laboratories had been certified—excluding physician labs, group practice labs or radiological offices which need no certification—and that a letter would be sent out from Social Security soon informing physicians of those laboratories which had been certified in California and out of state. After 15 May, Mrs. Kahn said, no payment under Medicare can be made to a laboratory if it is not certified.

23. *American Medical Association*

Mr. Gould, western field representative for AMA, informed the Council of a new proposal from the Internal Revenue Service which would tax advertising revenue of a tax-exempt organization derived from journal publication. He said the regulations were printed in the *Federal Register* 13 April. He reported that AMA was watching this closely, for it affects their revenue greatly. He also mentioned the matter of disability insurance and said that it is being re-studied by an AMA committee chaired by Doctor Appel. The results of this study will be brought before the AMA Board of Trustees some time in May. The Board will make recommendations and the proposals will be made to the House of Delegates in June.

24. *California Hospital Association*

President Henry Jackson reported that CHA had taken positive steps to try to improve the Medicare reimbursement formula. The recent approach, he said, had been to Congress to either reinterpret existing legislation or develop new. He said that CHA had been working with California Congressmen and key members of the House Ways and Means Committee regarding the hearings on HR 5710. Mr. Jackson also reported that the Health Manpower Council had not formally met with its permanent membership as yet. He also said that efforts were being made to create an ef-

fective data collection center by a tentative governing body of 12 members. He said that proposals had been sought from 10 computer-oriented firms, and were ready for review by the joint committee. Mr. Jackson extended his own personal appreciation and that of CHA to outgoing CMA President MacLaggan and Council Chairman Anderson for their cooperation and effective leadership, and offered the continued cooperation of CHA to the new incoming officers.

25. *Woman's Auxiliary to the CMA*

President Dorothy Bacon expressed her appreciation for all of the kindnesses shown her during her term of office.

26. *California Nurses' Association*

Mrs. Mary Stanley, past president, reported on the recent convention of the CNA and said that the Association was most happy to have Doctor MacLaggan and Mr. Henry Jackson at their banquet. She said that the CNA task forces to study the whole area of health manpower met together at an orientation meeting. From now on the task forces will meet separately. She said that there were representatives present from CMA, CHA, two LVN organizations, California League for Nursing and the Board of Nursing Education.

27. *California Medical Assistants Association*

Miss Helen Goldman, the new president of CMAA, briefly explained their education program which encompasses two levels of training. One program is designed for those who are already working in the field—in continuing education. The other level of education is preemployment education which, Miss Goldman said, is receiving more and more interest. She explained that this area has been under consideration for the past five years, and recently a statewide Advisory Committee on Medical Assistant Education was formed. The Committee advocates a two-year program with both theoretical and practical experience.

28. *California Coordinating Committee on Regional Medical Programs*

Director Paul Ward reviewed briefly the site visits and pending projects under the Heart Disease, Cancer and Stroke grants. He said it appeared that the projects would be approved virtually as submitted and outlined the various geographic areas of some of the project activities.

29. *Scientific Board*

Doctor Longmire, Chairman of the Scientific Board, reported on its recent meeting at which time the Millis and Coggeshall reports were taken under consideration. Doctor Longmire enumerated some of the recommendations of the Board regarding the Millis report. He said that it was felt that each training hospital should accept the responsibility of training and education as a corporate responsibility of the institution and should contribute to the program on a voluntary basis. It was also recommended that programs of graduate medical education not be approved unless the teaching staff, the related services and other facilities were judged adequate in size and quality, and that if these tests were met, approval be given formally to the institution rather than to a particular medical or surgical service most directly involved. Another recommendation stated that internship and residency should be combined into a single period of graduate medical education called a residency and planned as a unified whole. He said that the committee felt that the overall period of training should not be reduced, however. Finally, the committee recommended the creation of a Commission on Graduate Medical Education specifically for the purpose of planning, coordinating and periodically reviewing standards for graduate medical education and procedures for reviewing and approving institutions in which that education is offered. Regarding the Coggeshall Report, Doctor Longmire reported that the Board did not feel any specific report should be made but it did adopt the following statement:

"That the Council of the CMA transmit to the Trustees of the AMA and to the Council on Medical Education of the AMA, its belief that the practicing members of the medical profession have a deep and continuing interest in premedical, medical, and postgraduate and continuing medical education, and that practicing members of a profession are really the only individuals qualified to evaluate the professional competence of a person entering that profession. Any standards of evaluation employed should be national standards. It should not be the prerogative of each university to establish its own requirements for professional proficiency."

The Council received the report of the Scientific Board as well as its statement on the Coggeshall Report.

ACTION: *Voted to transmit the statement of the*

30. *Commission on Professional Welfare*

In the absence of Chairman Herzog, Mr. Whelan of the CMA staff reported to the Council. He outlined some of the recommendations that had been made for changes in the CMA retirement program (Keogh Plan). He said that these were being considered and a full report would be made to the Council at its next meeting.

Mr. Whelan also reported on the malpractice insurance study being undertaken by the Commission. He stated that a survey questionnaire has been developed and pretested by the Bureau of Research and Planning on 100 physicians, and that a detailed report would be available at the next Council meeting.

31. *Committee on Legislation*

Chairman Kilroy reported on various bills pending before the State Legislature. A number of these were considered by the Council.

32. *Committee on Scientific Information*

Discussion was initiated on the desirability of retaining the *function* of the Committee on Scientific Information, even though the committee is disbanded. It was pointed out that the committee function should be aimed toward physician as well as public education.

ACTION: *Voted to refer the matter to the Committee on Organizational Review and Planning, in consultation with the Scientific Board, to report back to the Council with recommendations on how the function could best be continued.*

33. *AMA Disability Insurance Program*

After some discussion on the AMA Disability Insurance Program, it was suggested that the CMA retain an independent actuary to study the program, reviewing claims experience as well as actuarial soundness.

ACTION: *Voted to retain independent actuary to study the AMA Disability Insurance Program.*

34. *Ad Hoc Committee to Study Relations of CMA with Component Medical Societies*

The Council received and discussed a report from the ad hoc Committee to Study Relations of CMA with Component Medical Societies. No action was taken.

35. *Membership*

Thirty-eight applicants were voted election to Associate Membership: Barbara Bartle, Gloria H. Bentinck, John Francis Harris, Marvin W. Rosenweig, Alameda-Contra Costa County; Irving I. Moses, James C. Reavis, Kern County; J. Edward Berk, John W. Bushnell, Pierre Vahe Haig, Marcus S. Handler, Lowell E. Irwin, Ray L. McClure, Rollin K. McCombs, Eugene Rosenman, Paul Schaffer, David C. Stolinsky, Clarke B. Walsworth, Los Angeles County; Marilyn F. Hicks, Edward Vanderhoof, Marin County; Charles Allen, Arnold Settlege, Napa County; Thomas Francis Judefind, Riverside County; Robert T. Gardner, Sacramento County; Patricia M. C. McIntyre, Lawrence D. Townsend, James R. Zier, San Diego County; Wallace V. Epstein, Angela Quilici, Alyce Tarcher, San Francisco County; Plimpton Gupstill, San Luis Obispo County; Ellis N. Cohen, Grant Fletcher, Jordan Katz, N. Ty Smith, Jesselene H. Thomas, Santa Clara County; Serafin Mabanag, Sidney L. Sattenstein, Stanislaus County; J. Austin Daly, Ventura County.

Forty-three members were voted election to Retired Membership: Markley C. Cameron, Geza J. Kertesz, Helen McGregor, Los Angeles County; Anne L. Brady, Marin County; Clarence Roland Kroeger, Mendocino-Lake County; Mildred F. Wehrly, Orange County; Percy A. Staley, Riverside County; Elmer M. Bingham, Thomas M. Manley, San Diego County; Ernest F. Gianotti, San Francisco County; Ralph J. Gampell, Santa Clara County; Edith Mythaler, James E. Thompson, Stanislaus County; Marine Ruffner Warden, Ventura County; Robert Loyhed Pye, Yolo County.

Reduction of dues was voted for 28 members for reasons of prolonged illness or postgraduate education.

36. *Roll Call*

Present were President MacLaggan, President-Elect Morrison, Speaker Quinn, Vice-Speaker Telford, Secretary Weyrauch, and Councilors Anderson, Dwight Wilbur, Isenhour, Eastman, Melone, Todd, Gooel, Taw, Bullock, O'Connor, Ham, Rogers, Crum, Boyle, Maguire, Burnett, Richard Wilbur; Miller, Watts, Fenlon, Kay, Kaiser, Yant, Grunigen, Longmire and Immediate Past-President Teall.

Present by invitation were CMA staff members Becker, Belser, E. Collins, J. Collins, Curley,

Eberlein, Goldman, Griffith, Hetland, Jones, Klutch, Lemos, Miller, Price, Redfern, Thomas and Whelan; Messrs. Hassard and Huber, legal counsel; component society executives Scheuber of Alameda-Contra Costa, Rideout of Butte-Glenn, Garrick of Forty First, Lingerfelt of Fresno, Geisert of Kern, Brock of Imperial, Dalbec of Los Angeles, Sower of Marin, Colvin of Monterey, Bannister of Orange, Walters of Riverside, Dochterman of Sacramento, Donmyer of San Bernardino, Nute of San Diego, Neick of San Francisco, Thompson of San Joaquin, Wood of San Mateo, Marvin of Santa Barbara, Donovan of Santa Clara, Brown of Sonoma, and Bruce of Tulare; Messrs. Paton, Babb, Bentley, Clark, Heller, Koch and Potloff of California Blue Shield; Messrs. Read, Brown, Putnam and McWilliams of the Public Health League; Doctor Dillon of UCLA, Doctor Egeberg of USC, Doctor Bostick of UC-CCM, and Doctor Tupper of UC, Davis; Doctor Rosen of the Office of Health Care Services; Doctor Breslow of the State Department of Public Health; Doctor Skelly of the State Department of Social Welfare; Doctor Lowry of the State Department of Mental Hygiene; Mr. Howard and Doctor Young of the State Department of Rehabilitation; Doctor Radl of the State Department of Employment; Mr. Spencer Williams, State Health and Welfare Agency; Mr. Henry Shine, State Department of Professional and Vocational Standards; Mrs. Mercia Kahn and Mr. Olsen, Bureau of Health Insurance, Social Security Administration; Mr. Gould of the American Medical Association; Mr. Layton of AMPAC; Mrs. Samuel K. Bacon of the Woman's Auxiliary to the CMA; Miss Helen Goldman of California Medical Assistants Association; Mr. Jackson of the California Hospital Association; Mrs. Mary Stanley and Mrs. Helen Hancock of the California Nurses' Association; Mr. Ward of the California Coordinating Committee on Regional Medical Programs; Congressman Ed Reinecke; and Doctors Ackerman, Doyle, Elliott, Epstein, Feldmyer, Gerrie, A. Howard, Kilroy, Klinger, Moore, Rosenbaum, Petit, Pheasant, Schor, Shipp, Steinberg, Willett and Wood; and Mrs. Carl Anderson.

37. *Adjournment*

The meeting was adjourned on Wednesday, 19 April at 8:55 a.m.

CARL E. ANDERSON, M.D., *Chairman*
HELEN B. WEYRAUCH, M.D., *Secretary*

532nd Meeting

Tentative Draft: Minutes of the 532nd Meeting of the Council, Los Angeles, Biltmore Hotel, 19 April 1967.

The meeting was called to order by President Morrison in the Biltmore Hotel, Los Angeles, on Wednesday, 19 April 1967 at 2:10 p.m.

Roll Call

Present were: President Morrison, President-Elect Todd, Speaker Quinn, Vice-Speaker Boyle, Secretary Weyrauch, and Councilors Dwight Wilbur, Moore, Eastman, Melone, Gooel, Shapiro, Bullock, O'Connor, Pheasant, Rogers, Crum, Maguire, Burnett, Richard Wilbur, Miller, Watts, Fenlon, Kay, Kaiser, Yant, Grunigen, Rose, Longmire and Immediate Past President MacLaggan.

A quorum was present and acting.

Present by invitation were CMA staff members Thomas, Collins and Redfern; Legal Counsel Hassard, and others.

1. *Election of Officers*

On nominations duly made and seconded, the following were unanimously elected to the positions shown: Chairman, Albert G. Miller; and Vice-Chairman, Harold Kay.

2. *Administrative Appointments*

On nominations duly made and seconded, the following were unanimously appointed to the positions shown: Secretary, Helen B. Weyrauch; Editor, Dwight L. Wilbur; Executive Director, Howard Hassard; and Legal Counsel, Peart, Hassard, Smith & Bonnington.

3. *Associate Editor of CALIFORNIA MEDICINE*

After brief discussion about creating the position of Associate Editor for CALIFORNIA MEDICINE, the Council made the following decision.

ACTION: *Voted to ask the Editor of CALIFORNIA MEDICINE, in conjunction with the Committee for Emergency Action, to submit a recommendation for filling the position of Associate Editor. (Editor to act as Chairman of the Nominating Committee.)*

4. Election of Councilors

The election of Fourth District Councilors to assume the positions vacated by President-Elect Todd and Vice-Speaker Boyle was deferred until the next regular meeting. At that time recommendations for the positions will be made by the Los Angeles County Medical Association.

ACTION: *Voted to re-elect Doctor Forest J. Grunigen to represent the Twelfth District (Forty-First Medical Society).*

5. Committee Appointments

Chairman Miller, on nominations presented by the Committee on Committees and the Council concurring, made the following committee appointments:

Bureau of Research and Planning—Carl E. Anderson, Chairman, Santa Rosa; J. Brandon Bassett, Oakland; G. Robert Ellison, Pomona; H. Russell Fisher, Glendale; John Sheehy, Riverside. Ex-Officio—Malcolm S. M. Watts, San Francisco; Jean Crum, Downey.

Committee on Role of Medicine in Society—Malcolm S. M. Watts, Chairman, San Francisco; Gerald Besson, Sunnyvale; Burt L. Davis, Palo Alto; Sanford Feldman, San Francisco; Elmer Gooel, Beverly Hills; Sherman Mellinkoff, Los Angeles; Malcolm C. Todd, Long Beach. Ex-Officio—Carl E. Anderson, Santa Rosa; Jean Crum, Downey.

Committee on Organizational Review and Planning—Jean Crum, Chairman, Downey; Robert Hood, Van Nuys; H. Dean Hoskins, Oakland; John Rumsey, San Diego; John Saidy, San Mateo; Ralph C. Teall, Sacramento; Charles John Tupper, Davis. Ex-Officio—Carl E. Anderson, Santa Rosa; Malcolm S. M. Watts, San Francisco.

Liaison Committee to CPS—John G. Morrison, San Leandro; Malcolm C. Todd, Long Beach; William F. Quinn, Los Angeles; Albert G. Miller, San Mateo.

Professional Advisory Committee to University of California, California College of Medicine—Forest J. Grunigen, Los Angeles.

Committee on Legislation—Dan O. Kilroy, Chairman, Sacramento; Stuart C. Knox, Los Angeles; John Rumsey, San Diego; Samuel R. Sherman, San Francisco; Harold E. Wilkins, Downey. Ex-Officio—John G. Morrison, San Leandro; Malcolm C. Todd, Long Beach; Albert G. Miller, San Mateo; William F. Quinn, Los Angeles.

Benevolence Fund Operating Committee—Clyde L. Boice, Chairman, Palo Alto; Dudley M. Cobb, Jr., Los Angeles; Alexander Fraser, San Francisco; Elizabeth Mason Hohl, Los Angeles; Frank C. Melone, Ontario; Don C. Musser, San Francisco; George Wolf, Fresno.

Advisory Board to Woman's Auxiliary—John G. Morrison, San Leandro; Malcolm C. Todd, Long Beach; Fred Ackerman, Pleasant Hill; James C. MacLaggan, San Diego; Ralph C. Teall, Sacramento.

Finance Committee—Harold Kay, Chairman, Oakland; Henry V. Eastman, Tustin; Elmer Gooel, Los Angeles; Frank C. Melone, Ontario; Marvin Shapiro, Encino.

Committee on Committees—Malcolm C. Todd, Chairman, Long Beach; Ralph W. Burnett, Bakersfield; William F. Kaiser, Berkeley; Joseph P. O'Connor, Pasadena; Malcolm S. M. Watts, San Francisco; Henry V. Eastman, Tustin; Richard S. Wilbur, Palo Alto; James H. Yant, Sacramento; Wilbur G. Rogers, Glendale; John G. Morrison, San Leandro; William F. Quinn, Los Angeles; Albert G. Miller, San Mateo; James C. MacLaggan, San Diego.

CMA Representatives on the Joint Council to Improve Health Care of the Aging—Thomas El-mendorf, Willows; Joseph P. O'Connor, Pasadena; Pierre Salmon, San Mateo; Charles E. Schoff, Jr., Sacramento.

CMA-CHA Advisory Board—Bert L. Halter, San Francisco; James C. MacLaggan, San Diego; Glenn A. Pope, Sacramento; John T. Saidy, San Mateo; Joseph W. Telford, San Diego; John G. Morrison, San Leandro; Malcolm C. Todd, Long Beach; Albert G. Miller, San Mateo; William F. Quinn, Los Angeles.

CMA Councilors on CPS Board of Trustees—Roberta Fenlon, San Francisco; Wilbur G. Rogers, Glendale; James H. Yant, Sacramento.

Council Designees (2) on Scientific Board and Executive Committee—Lewis T. Bullock, Los Angeles; Malcolm S. M. Watts, San Francisco.

Advisory Committee to CMA Representatives on Regional Medical Programs—Malcolm S. M. Watts, Chairman, San Francisco; L. B. Blanchard, San Jose; Harold I. Griffeath, San Francisco; Donald W. Petit, Los Angeles; David Rubin, Los Angeles; Saul Robinson, San Francisco; Justin J. Stein, Los Angeles; David A. Wood, San Francisco.

CMA Representatives to Interagency Council on Smoking and Health—Gerald Hill, San Rafael; James Kieran, Berkeley.

Subcommittee on Industrial Medical Fees—Roger C. Isenhour, Chairman, San Diego; H. Dean Hoskins, Oakland; Homer C. Pheasant, Los Angeles.

CMA Appeals Committee—Homer C. Pheasant, Chairman, Los Angeles; George Babbitt, Sacramento; Leo Bell, San Mateo; Joseph F. Boyle, Los Angeles; Ralph Burnett, Bakersfield; Albert G. Clark, San Francisco; Thomas N. Elmendorf, Willows; Wallace A. Gerrie, Jr., Newport Beach; H. Dean Hoskins, Oakland; Arthur F. Howard, Fresno; Roger C. Isenhour, San Diego; Eli A. Layon, Brawley; Alfred J. Murrieta, Jr., Los Angeles; Leonard R. Ortega, Oakland; Glenn A. Pope, Sacramento; Maurice S. Salomon, San Francisco; Richard L. Taw, Los Angeles; Robert L. Taylor, Oakland; William H. Thompson, San Mateo; Robert L. Watson, Jr., Los Angeles; Milo A. Youel, San Diego.

Industrial Medical Committee—John G. Morrison, San Leandro; Malcolm C. Todd, Long Beach; Albert G. Miller, San Mateo; Howell E. Wiggins, San Diego; Roger C. Isenhour, San Diego.

Liaison Committee to California Medical Assistants Association—Charlotte Baer, San Francisco; Peary Benn Berger, Inglewood; Henry Bodner, Van Nuys; Leland W. Bonar, Redding; Michael F. Brodtkin, Beverly Hills; Sanford E. Feldman, San Francisco; William H. Forestelle, Seaside; Richard H. Schug, Long Beach.

Committee on Continuing Medical Education (to Scientific Board)—*Area Representatives*—Thomas J. Fuson, Fresno; K. M. Joye, Auburn; A. F. Kandlbinder, Monterey; Robert H. Quillinan, Sacramento; Robert S. Quinn, Santa Rosa; Edward Shanbrom, Santa Ana; Raymond Tatrow, San Bernardino; J. Roy Wittwer, Eureka; George J. Wittenstein, Santa Barbara.

Subcommittee on Venereal Disease (of Committee on Public Health)—Horace F. Sharrocks, Chairman, Sebastopol; Thomas E. Jones, Fullerton; Willard M. Meininger, Sacramento.

District Committees on Maternal Mortality Review—*District I*—Joseph M. Botte, Chairman, San Diego; J. L. Heard, San Diego; Bruce Jessup, Berkeley; Hobart M. Kelly, Riverside; Ralph M. King, La Mesa; Paul Peterson, Fullerton; Roger

W. Ridley, Riverside; Sid Saltzstein, San Diego; B. Glenn Smith, Riverside; Emma Wharton, Santa Ana.

District II—Bruce B. Rolf, Chairman, Los Angeles; Gene Ray Bouch, Long Beach; John W. Budd, Los Angeles; Kenneth Chapman, Los Angeles; Marvin Darsie, Jr., Santa Monica; Harlan Ellis, Los Angeles; George Harris, Beverly Hills; Lester T. Hibbard, Los Angeles; Robert F. Kelly, Los Angeles; George A. Macer, Pasadena; Sakaye Shigekawa, Los Angeles; Scott Whitehouse, Los Angeles; Bruce Jessup, Berkeley.

District III—Leon P. Fox, Chairman, San Jose; Bramwell R. Anthony, San Luis Obispo; John C. Bodle, Santa Rosa; James R. Dickson, Los Gatos; Antonio J. Franz, San Francisco; Logan Gray, San Mateo; Arthur C. Hemphill, Napa; Karl E. Kirschner, San Luis Obispo; Victor E. Koerper, Oakland; Lester G. Krotcher, San Francisco; Paul A. Roach, Santa Cruz; Gilbert A. Webb, San Francisco; Bruce Jessup, Berkeley.

District IV—Nicholas W. Demas, Chairman, Stockton; A. C. Armanini, Jr., Stockton; James J. Benn, Jr., Ripon; Willard Fisher, Tracy; Lee D. Fulton, Redding; Robert M. Hutt, Stockton; John T. McNally, Stockton; Warren Plowman, Lodi; Dale W. Ritter, Chico; Robert S. Westphal, Modesto; Bruce Jessup, Berkeley.

District V—Robert A. Vaughan, Chairman, Fresno; Frank L. Davidson, Fresno; Harlan F. Fulmer, Fresno; Arthur F. Howard, Fresno; James B. Peery, Fresno; Hall Ramirez, Bakersfield; William Sidders, Bakersfield; Bruce Jessup, Berkeley. Consultant: Patricia Henderson, Fresno.

6. Search Committee

On nominations duly made and seconded, the following were appointed to serve on the Search Committee: Wilbur G. Rogers, Chairman, Ralph W. Burnett, James H. Yant, James C. MacLaggan, and John G. Morrison.

7. Time and Place of Next Meeting

The chairman announced that the next regular meeting of the Council would be held in San Francisco (Hilton Inn) on Saturday, 27 May 1967.

8. Adjournment

There being no further business to come before it, the meeting was adjourned at 2:50 p.m.

ALBERT G. MILLER, M.D., *Chairman*
HELEN B. WEYRAUCH, M.D., *Secretary*

A New Relationship with Government and Others

A Report by the Committee on the Role of Medicine In Society, California Medical Association

THE ENACTMENT OF Public Law 89-97 was a milestone in the progress of involvement of government in health care in this nation. This law gives legal expression to the widely proclaimed social principle that health care has now become a personal right of every citizen. In so doing, it has placed health care among those individual rights which are subject to guarantee by the power of government. The legislative decision has fundamentally altered the relationships between medicine and government. The California Medical Association Committee on the Role of Medicine in Society in this report seeks to examine various aspects of these altered relationships and to make some suggestions with respect to what might be required if medicine is to continue to play an effective role in the changed environment of medical care.

Some Experiences Abroad

Considerable experience with the problems which can result from government involvement in personal health care has been accumulated in many nations abroad. As of May 1964, 64 countries throughout the world, including all European nations, had some type of government sickness insurance or benefit program which in one way or another involved government in personal medical care. The "Professional Problems Associated with Federalized Health Care" experienced in a

This is the second of three articles by the Committee on the Role of Medicine in Society that have been received by the Council and the House of Delegates of the California Medical Association. No official action has been taken on them by either body and they are being published here as they were received by the Council and the House of Delegates, for information.

The first article, "Responsibility for Quality in Health Care," was printed in the June 1967 issue of *California Medicine*, and the third, "Organizing for Health Care," is scheduled to appear in August.

Reprint requests to: California Medical Association, 693 Sutter Street, San Francisco 94102.

number of these nations were examined in a *Socio-Economic Report* (Vol. V, No. 11, October 1965) of the CMA Bureau of Research and Planning. The principal problems, all of which have profound impact upon the quality of health care received by the patient, were found to be the following (listed approximately in the order of their occurrence):

(1) *Inadequate Physician Remuneration*

This has been found to cause expensive and wasteful practices in patient care as well as exerting an adverse influence on physician motivation.

(2) *Decline of Professional Status and Subsequent Authority of Physicians*

It should be pointed out that the doctor gives advice, not orders, to patients, and if results are to be achieved the patient must have sufficient faith and confidence in the doctor to be willing to follow the advice. Where this professional status and authority of the doctor is undermined the effectiveness of patient care becomes seriously compromised.

(3) *Dominance of Political Decisions in Allotting Funds*

Experience has shown that this often results in inadequate funding of health care programs, to the detriment of high quality patient care.

(4) *Bureaucracy of Federal Control*

The responsibility to control the expenditure of public funds can lead to a cumbersome bureaucratic system which requires medical care to be adapted to the mechanics of a system which may or may not meet the needs of the patient.

(5) *The Patient's Perspective:*
Impersonality of Care

In many foreign programs the physician has become an overworked professional, not particularly interested in the personal problems of the patient, who often has little privacy, long waits for service and little to say about his own care.

These experiences abroad are cited only to draw attention to a number of problems which have occurred elsewhere and which must be avoided if possible as the government of this nation becomes more involved in health care. A major aim of the new relationships which are to be developed between medicine and government should be to prevent or to resolve any such problems before they affect patient care adversely.

"Partnership"—A Suggestion From Government

It has been proposed by some highly placed federal officials that medicine enter into a "creative partnership" with government in a collaborative effort for better health care. The proponents envision that this "partnership" would be one of many cooperative relationships between the federal government and state and local governments and between the federal government and the private sector. Taken together, these would comprise a "creative federalism" or the "new concepts of cooperation" which have been proposed by President Johnson. Secretary Gardner has stated that "in the Department of Health, Education and Welfare—perhaps more than in any other—"creative federalism" is becoming a day-to-day reality."¹ Vice President Hubert H. Humphrey has said: "I invite American medicine to come forth with its constructive suggestions. Let the executive and legislative branches hear your expert views. Let us improve whatever needs improving. Let us be genuine working partners."² Since the enactment of PL 89-97 the federal government has clearly recognized in many tangible ways that the cooperation and help of American medicine is essential if the new federal programs are to be made to work. American medicine, including much of the health care industry, has given substantially of time, talent and also substance in a giant collaborative effort to put these new health care programs into operation on schedule and to make them workable. The combined effort has so far been successful beyond all expectations. But the task

is a continuing one and the on-going relationships are still largely ill-defined.

A Statement of Strengths and Capabilities

The Committee believes that any on-going working relationship between medicine and government should be based upon a full recognition of the strengths and capabilities of each as they might influence or be influenced by the other.

It is suggested that the basic strength of government's position lies in the following:

(1) Public acceptance of the proposition that health care is a personal right to be guaranteed to all citizens along with other personal rights.

(2) The precedent of government involvement in health care by reason of its financial support of research, construction of facilities for health science and health care, and patient care for various categories of eligible persons.

(3) The responsibility of government to exercise supervision and control over the expenditure of public funds.

(4) The power of compulsion, the police power upon which all the resources and activities of government are ultimately based.

It is suggested that the basic strength of medicine's position lies in the following:

(1) The medical profession renders an essential service to society and has the most direct knowledge of what is involved in, and the most direct responsibility for, the care of patients.

(2) The effectiveness and quality of this service depends upon the skill and motivation of the physician and the allied health professionals.

(3) Progress and improvement in health care requires that both the incentive and the freedom to try new methods in patient care be present.

(4) There is a tacit recognition of the principle that it is better to have the physician and the health professional working for the patient rather than for the government.

(5) The medical profession has the capacity to exercise the most effective supervision of its members.

The strengths of the government position are therefore firm and quite tangible while those of medicine are more fragile and often quite intangible. The government position is founded upon the law, is directed toward the "public interest" and in the final analysis enforced by compulsion. Medi-

¹John W. Gardner, "Creative Federalism," *Health Education and Welfare Indicators*, October 1966.

²*Medical World News*, 2 September 1966, p. 59.

cine's position, on the other hand, rests upon the skill and motivation of the health professional, is directed to the individual patient's interest, and derives its public support from good performance which is understood and appreciated. Each has a capability to influence the other. The new relationships between medicine and government will be determined by the way in which these strengths and capabilities are developed and used.

Confrontation, Partnership or Teamwork?

It is the common aim of both medicine and government to make the highest quality of health care available to every citizen. However, it is in the nature of government to place the common good, the "public interest," above the individual interest whenever the two conflict, and it is in the nature of medicine always to give primacy to the individual and his particular needs. It is when the "public interest," as defined by government, conflicts with the patient care interest as defined by medicine that difficulties are apt to arise. Unless these conflicts are prevented or resolved at an early stage, experience indicates that destructive confrontations can occur. As the new relationships between medicine and government are developed, a major purpose should be to insure sufficiently close collaboration so that at all times there will be agreement on the means by which the common aim is to be achieved and thus damaging confrontations can be avoided.

It was no doubt a recognition of this need for collaboration which led the American Medical Association, after enactment of the legislation, to offer any assistance it could give to the federal government in developing the "medicare" regulations. This same recognition, no doubt, gave rise to the invitation from government to medicine to join in a "creative partnership" for better health care. While it seems unlikely that any formal regulation of the "partnership" is intended by the government proponents, the fact remains that any sort of partnership which binds one to a partner who possesses the ultimate power of compulsion would in the end be no partnership at all.

The Committee believes the word "teamwork" more appropriately describes the relationship which should develop between medicine and government. Webster defines this as "work done by a number of associates each doing a part but all subordinating personal prominence to the efficiency of the whole." Teamwork in this definition can achieve and has accomplished much in our

pluralistic society. The concept respects the identity and worth of each member of the team and also maintains a focus upon the common goal which they seek to achieve together.

Teamwork in a Pluralistic Society

The American tradition is that of a pluralistic society, a society in which members of diverse social groups maintain their autonomy while at the same time making their special contributions to the development of a common culture or civilization. In such a society it is important that opposing ideas or values not only be recognized but that they be encouraged and stimulated. The greatest good for the society as a whole is achieved through the sharing of different viewpoints which are communicated, interpreted, comprehended, modified and applied so that society may derive the maximum benefit from each as it undergoes necessary change. This creative approach to planning and action is quite distinct from a "planned" economy in which the interests and contributions of all groups are subordinated to, and may not even be considered by, the single segment (usually government) which dominates the planning process or action program.

There can be no question that the federal health legislation now enacted into law contains the seeds of a "planned" economy in health care with the potential of absolute federal control of almost every aspect of health care. While it is recognized that this federal control may be the wish or expectation of some who are highly placed in the federal government, there are nevertheless many responsible federal administrators who have indicated a real desire to avoid federal domination and to develop genuine and effective cooperative efforts with non-federal agencies or groups to improve health care. The Committee believes that it is imperative that the intent of these administrators be made to prevail and that it is incumbent upon medicine to do everything within its power to make genuine effective cooperative effort a practical reality. Teamwork in a pluralistic society is the best means to achieve the common aim of all to make even better health care available to every person.

Constructive Leadership from CMA

The Committee finds that the California Medical Association has taken many significant actions and has developed a substantial number of creative programs which have earned for it a reputation

for constructive leadership. It has shared its expertise and experience with government and many others who seek good solutions for the scientific, social, economic and political problems inherent in providing ever better health care. It is unfortunate that the nature, scope and effectiveness of these efforts to date are not more generally known by the CMA membership or appreciated by the public. The Committee also finds that much of this successful collaborative accomplishment in California may also properly be ascribed to the high caliber of leadership in government and elsewhere within this state which has generally utilized to good advantage the federal and state funds available for health sciences and health care, and to a genuine willingness on the part of a substantial number of these leaders to work closely with medicine and the health care industry. It is this background of experience which places the CMA in a singularly advantageous position at this time to exercise important and constructive leadership in helping to shape the new relationships of medicine with government at all levels.

Developing Strength for Medicine's Position

If the concept of teamwork within the framework of the traditional American pluralistic society is to dominate the new relationships of medicine with government, it is essential that medicine be in a position to make a strong and effective contribution to the overall effort. The Committee believes that it will take strength—perhaps power is actually a better word—for medicine or any group to be able to contribute effectively to a team, one of whose members is the government with all its massive powers, and at the same time maintain the autonomy and independence which will insure that its contribution will be worthwhile, and also that the overall approach can continue to be a pluralistic rather than a “planned” economy. The Committee believes that it is now incumbent upon medicine and particularly upon the CMA to identify and deliberately seek to strengthen its capability for overall effectiveness in health care. It is suggested that further strength must be developed in each of four areas.

1. Knowledge of Health Care

There is a body of knowledge and expertise which is beyond the experience of the average practicing physician but which medicine must somehow understand if it is to make its most effective contribution to the advancement of health care

in present-day society. The practicing physician has unmatched knowledge of what is involved in the art and science of individual patient care but he may have something to learn about the social and economic practicalities involved in prevention, health maintenance and rehabilitation, and in the availability and delivery of high quality health care. On the other hand, it is equally true that a labor leader, a social scientist, a consumer representative or a government physician, any of whom may perhaps be well-informed on many of the socioeconomic complexities of the delivery of health care, is unlikely to be knowledgeable about all that is involved in rendering day-to-day high quality care to individual patients. It is therefore essential that medicine become as knowledgeable as possible about the “non-professional” aspects of health care and develop a base of uncontested fact and experience from which it can make timely and effective presentation of its expert views. Knowledge is power, whether it be in patient care, computer technology, socioeconomic research or in political science as they pertain to various aspects of health care. Medicine cannot afford to leave this area of research and study entirely to others.

The CMA Bureau of Research and Planning is a pioneering effort by organized medicine which has already enormously strengthened the contributions of CMA and its leaders by providing them with facts and information which have enabled medicine to play a positive role with government and others who seek better health care in California. The Committee views the CMA Bureau of Research and Planning as a prototype of what must be created as soon as possible within organized medicine as a whole in order to develop and make easily available the body of knowledge which physicians and their leaders must have if medicine is to play its most effective role in its new relationships with government, the health care industry and other voluntary agencies and organizations.

2. Involvement

Medicine renders an essential service in patient care but this service, essential as it is, constitutes a relatively small proportion of the totality of health care. The essential contribution of medicine consists of its art and science. There are some in medicine who advocate that medicine restrict its concern and contribution to this and adopt a policy of watchful waiting and of “being available” for

consultation by government and others. The Committee, however, believes that medicine has much more to offer to the advancement of health than simply its professional technology, and furthermore that it is now necessary for medicine to participate more broadly in the totality of health care if only to help create and maintain social, economic and political conditions which will permit the art and science to flourish and be practiced effectively in the best patient interest.

Experience has shown that involvement is an important tool for power and influence in a pluralistic society. It is a most effective way to introduce a viewpoint so that it can be heard, communicated, interpreted, comprehended, modified and applied. Involvement means that people involve themselves and their organizations with others to solve problems. Involvement in collaborative effort can and has influenced government. Involvement includes the planning process, decision-making and program implementation. There can be little question that involvement means power in a pluralistic society. There can be no question that medicine—physicians, their representatives and their professional organizations—must become intimately involved if a pluralistic approach to better health care is to work effectively in the total society.

CMA has already accomplished much through the understanding and collaboration which has resulted from involvements of many sorts. This has been a major source of CMA influence and has proved its success. The Committee believes the process of involvement should now be used on a wider scale wherever there is opportunity and proper indication.

3. Financial Support

Adequate financing is essential if CMA or medicine as a whole is to make the kind of positive contribution it should and must to a pluralistic approach to health care, and at the same time strengthen and maintain the autonomy and independence of organizational medicine which is essential to this purpose. Physicians generally recognize the importance of supporting their professional associations and no doubt will continue to do so. However, it seems unlikely that the dues structure can support all of the functions which will be necessary. Other funding will be necessary for many activities.

The Committee believes that adequate financing must be developed to support the role of medicine and particularly of the CMA, an independent and

autonomous organization, as they become ever more active and effective participants in the totality of health care in California. This will require a realistic appraisal of the possibility of utilizing funds from a number of sources other than membership dues. There have already been beginnings and some precedents have been established. Funds from a number of organizations may be pooled, contracts entered into, or grants received from public or private sources to perform services or research or otherwise accomplish purposes which are of interest to all the parties concerned. The Committee suggests that the use of grants has proved quite acceptable and effective in many areas of education, research and health care, and that properly designed grants from both public and private sources have proved to be mutually advantageous and not to compromise the integrity, autonomy or independence of the grantee. Adequately financed support is essential to the strength of medicine's position and much will depend upon how well alternative methods of financing are developed and used.

4. Public Understanding and Support

Public opinion is a potent influence on government and upon society as a whole, and experience has shown that to ignore public opinion is to court disaster. Medicine has been curiously blind to this reality and has made little effort to develop either public understanding or support for its worthwhile aims. The Committee believes that this public understanding and support must soon become a real strength instead of a weakness, if medicine is to be truly strong and effective in its relationships with government and other groups concerned with health and health care.

The Committee believes that medicine and particularly the CMA should give prompt attention to the elements which form public opinion and how it can become informed, and that a more aggressive effort should be made to apprise the public of the good performance of medicine and CMA in the public and patient interest. It is suggested that "public service" might well be the watchword. This emphasizes participation and collaborative effort in the best interest of people. Such a new approach will require new skills and new techniques as well as a less inhibited and more flexible use of those already at hand. It is essential that medicine become imaginative and successful in the development of public understanding and support. Medicine and CMA must recognize that this is

now a decisive political force in this nation and it will remain so for the foreseeable future. Involvement in the election and education of legislators is a most important responsibility of the medical profession.

A Basic Position for Medicine

As medicine enters into new relationships, not only with government but also with the rest of the non-governmental sector in health care, it is important that it identify a basic position from which it can make its most valuable contribution to the whole. This position should be based upon its assessment of its own strengths and capabilities in the changing environment of health care in the state and nation. It should recognize that medicine is most directly concerned with the circumstances and nature of the care actually received by the individual patient, and it should enable medicine to join with others who seek to avoid problems such as have developed in other nations when government has become directly involved in personal medical care.

The Committee suggests that the following guidelines may be useful for medicine and the CMA in establishing such a basic position:

1. The physician and the medical profession are most knowledgeable concerning what is involved in individual health care. The standards of quality should remain a responsibility of the health care professions. Voluntary professional mechanisms for the assessment and control of quality, including utilization, should be encouraged and made to function effectively in every aspect of patient care, including research and education.

2. The physician and the medical profession can constantly speak to and emphasize the need to recognize the individuality and personal dignity of human beings, the individuality of their needs in health maintenance and health care, and the importance of personal consideration, and even privacy, especially in times of illness or stress. Plurality of solutions to problems in health care should be encouraged and emphasis placed upon

the importance of tailoring any health care system to fit the needs of individual patients rather than the reverse.

3. In the inevitable conflict which is sure to arise between the need to cut health care costs on the one hand, and the need for the adequate funding from whatever source which will make high quality care possible on the other, the physician and the medical profession should stand firmly for adequate funding while at the same time cooperating with all concerned to prevent waste and inefficiency.

4. The physician and the medical profession should assume a major responsibility for keeping the public informed of the progress toward the common goal of making the best health care available to every citizen. They should publicly support the expressed intent of those government officials who have indicated a real desire to avoid federal interference with health care and to develop genuine and effective cooperative efforts with non-federal agencies or groups. They should take positive steps to help strengthen the overall contribution of the private sector in order that a reasonable balance between government and private enterprise may be maintained. They should be alert to any regulations or controls which might repress or suppress the incentive or freedom to experiment and explore new methods, which is the *sine qua non* of true progress, in health care, recognizing that the right to experiment or explore carries with it the right to succeed or to fail and of course must reasonably safeguard the rights of individuals as well as the public interest. Medicine's intent must be clear and it must be clearly communicated.

The Committee believes that aims such as these, if aggressively pursued in dialogue and in performance, can earn for medicine the support of health professionals, patients and the public, as well as the government, and thus make it possible for medicine to help strengthen the traditional American approach to the solution of problems, the approach which has made energetic freedom-loving people seek our shores, and made this nation what it is.

In Memoriam

ALEXANDER, ISAAC, Oakland. Died 11 May 1967, in Oakland, aged 83, of arteriosclerotic heart disease. Graduate of Jefferson Medical College of Philadelphia, 1910. Licensed in California in 1919. Doctor Alexander was a retired member of the Alameda-Contra Costa Medical Association and the California Medical Association, and an associate member of the American Medical Association.



ANDERSON, CLIFFORD RUSSELL, Glendale. Died 2 June 1967, in Glendale, aged 61, of astrocytoma. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1942. Licensed in California in 1944. Doctor Anderson was a member of the Los Angeles County Medical Association.



ANDREWS, VERNON LEE, Costa Mesa. Died 21 May 1967, in Costa Mesa, aged 92. Graduate of University Medical College of Kansas City, Missouri, 1906. Licensed in California in 1927. Doctor Andrews was a retired member of the Los Angeles County Medical Association and the California Medical Association, and an associate member of the American Medical Association.



BERGMANN, WERNER, Oakland. Died 14 May 1967 in Oakland of shock and hemorrhage due to trauma in a fall from a ladder, aged 52. Graduate of Universiteit van Amsterdam Geneeskunde Faculteit, Amsterdam, The Netherlands, 1939. Licensed in California in 1948. Doctor Bergmann was a member of the Alameda-Contra Costa Medical Association.



DOANE, BERT LEE, Los Angeles. Died 16 May 1967, in Beverly Hills, of peripheral vascular disease, aged 89. Graduate of Northwestern University Medical School, Chicago, 1905. Licensed in California in 1919. Dr. Doane was a member of the Los Angeles County Medical Association.



DOOLEY, ROBERT L., Pomona. Died 7 May 1967, in Pomona, aged 42. Graduate of the College of Osteopathic Physicians and Surgeons, Los Angeles, 1952. Licensed in California in 1953. M.D. degree from California College of Medicine, 1962. Doctor Dooley was a member of the Los Angeles County Medical Association.



ELLEFSON, OLLEY D., Turlock. Died 3 June 1967 in Turlock, aged 63, of heart disease. Graduate of State University of Iowa College of Medicine, Iowa City, 1927. Licensed in California in 1932. Doctor Ellefson was a member of the Stanislaus County Medical Society.



GODWIN, DEAN ELY, Long Beach. Died 30 May 1967, in Long Beach, aged 85, of pneumonia and leukemia. Graduate of the University of Michigan Medical School, Ann Arbor, 1909. Licensed in California in 1921. Doctor Godwin was a retired member of the Los Angeles County Medical Association and the California Medical Association, and an associate member of the American Medical Association.

GOIN, LOWELL SIDNEY, Los Angeles. Died 4 June 1967, in Los Angeles, aged 75, of myocardial ischemia with congestive failure. Graduate of St. Louis University School of Medicine, 1912. Licensed in California in 1926. Doctor Goin was a retired member of the Los Angeles County Medical Association and the California Medical Association, and an associate member of the American Medical Association.



HENDERSON, W. RAY, Garden Grove. Died 27 May 1967, in Newport Beach, aged 81, of cardiogenic shock. Graduate of Rush Medical College, Chicago, Illinois, 1927. Licensed in California in 1927. Doctor Henderson was a member of the Los Angeles County Medical Association.



JOHNSON, CHARLES OWEN, Gardena. Died 6 May 1967, in Gardena, aged 43. Graduate of State University of Iowa College of Medicine, Iowa City, 1951. Licensed in California in 1952. Doctor Johnson was a member of the Los Angeles County Medical Association.



MARTIN, MARSHALL LEE (M. LEE), LaVerne. Died 20 May 1967, in Pomona, aged 88. Graduate of the University of Southern California School of Medicine, Los Angeles, 1907. Licensed in California in 1907. Doctor Martin was a retired member of the Los Angeles County Medical Association and the California Medical Association, and an associate member of the American Medical Association.



MILLER, WILLIAM MCCARTNEY, Auburn. Died 24 February 1967, in San Francisco, aged 74, of carcinoma of the colon with metastasis. Graduate of Chicago College of Medicine and Surgery, 1916. Licensed in California in 1917. Doctor Miller was a retired member of the Placer-Nevada County Medical Society and the California Medical Association, and an associate member of the American Medical Association.



MUSICER, MORRIS H., Pico Rivera. Died 31 May 1967, in Inglewood, aged 53, of coronary artery disease. Graduate of the College of Osteopathic Physicians and Surgeons, Los Angeles, 1940. Licensed in California in 1940. M.D. degree from California College of Medicine, 1962. Doctor Musicer was a member of the Los Angeles County Medical Association.



PEGGS, HAROLD JARED, Santa Clara. Died 7 May 1967, in Los Gatos, aged 55. Graduate of the State University of Iowa College of Medicine, Iowa City, 1940. Licensed in California in 1961. Doctor Peggs was a member of the Santa Clara County Medical Society.



ROGERS, GEORGE G., San Francisco. Died 17 October 1966, at Veterans Home, Yountville, aged 70. Graduate of Jefferson Medical College of Philadelphia, Pennsylvania, 1924. Licensed in California in 1932. Doctor Rogers was a member of the San Francisco Medical Society.

SCHWALENBERG, HAROLD RAYMOND, Santa Barbara. Died 21 May 1967 in Santa Barbara, aged 72. Graduate of the University of California, Berkeley and San Francisco, 1926. Licensed in California in 1926. Doctor Schwalenberg was a member of the Santa Barbara County Medical Society. ❀

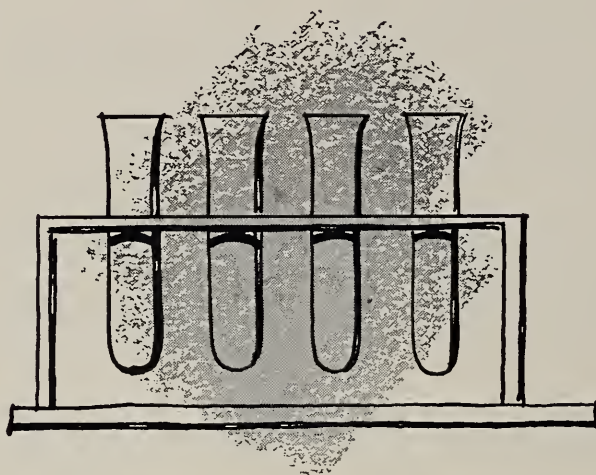
SHERY, KURT THOMAS, Torrance. Died 9 May 1967, in Torrance, aged 58, of heart disease. Graduate of Albertus-Universität Medizinische Fakultät, Königsberg, Prussia, 1933. Licensed in California in 1942. Doctor Shery was a member of the Los Angeles County Medical Association. ❀

SILLIPHANT, WILLIAM M., San Francisco. Died 29 May 1967, in San Francisco, aged 66, of cancer. Graduate of Stanford University School of Medicine, Palo Alto-San Francisco, 1931. Licensed in California in 1931. Doctor Silliphant was a member of the San Francisco Medical Society.

SWANSON, RALPH BUFORD, San Francisco. Died 26 May 1967, in Mill Valley, aged 35. Graduate of the University of Minnesota Medical School, Minneapolis, 1956. Licensed in California in 1957. Doctor Swanson was a member of the San Francisco Medical Society. ❀

TAYLOR, JOHN C. WALLACE, San Rafael. Died 23 May 1967, in San Rafael, aged 74. Graduate of Hahnemann Medical College of the Pacific, San Francisco, 1917. Licensed in California in 1917. Doctor Taylor was a member of the Marin Medical Society. ❀

WURTZ, REGINALD MATT, Palos Verdes Estates. Died 16 May 1967, in Torrance, of uremia, aged 50. Graduate of the University of Nebraska College of Medicine, Omaha, 1943. Licensed in California in 1949. Doctor Wurtz was a member of the Los Angeles County Medical Association.



PUBLIC HEALTH REPORT

Lester Breslow, M.D., M.P.H.

Director, State Department of Public Health

CALIFORNIA PHYSICIANS have been among the first to recognize that the prevention of air pollution is necessary for healthful life in cities. Local and state governments in California were among the first to propose remedies.

However, these remedies are sometimes complicated, costly and slow; occasionally they are uncertain. Eye and respiratory tract irritations are frequent effects of pollution with photochemicals. Many patients turn to their physicians because of these symptoms. Greater public understanding of these and other air pollution effects is essential to progress in air pollution control.

Since 1954, the State Department of Public Health and air pollution control districts have carried out monitoring programs which measure potentially harmful pollutants. These include carbon monoxide, oxidants, oxides of nitrogen and particulates. In addition the department in conjunction with medical scientists has carried out a program of laboratory and epidemiologic research.

Sufficient data have been collected about the effects of certain pollutants to permit the Health Department to set sound air quality standards. These standards are the basis for the present controls over motor vehicle emissions. These controls are increasingly being adopted, with some modifications, in other parts of the nation and of the world. This year, because of them and despite the increase in motor vehicle usage, emissions of carbon monoxide and hydrocarbons are decreasing in California.

As effects that pollutants may have on health, we now recognize the possibility of acute illness or death; the possibility of production of chronic disease; interference with important functions of the body; sensory irritation, and discomfort, annoyance, and impairment of visibility.

Air pollution during the acute episodes in California so far has not significantly increased mor-

talidity. This is unlike findings in eastern United States, Europe and Japan. While a specific acute illness associated with air pollution has not been shown, the aggravation of bronchitis and, of course, eye and respiratory symptoms are very well known.

A survey in Los Angeles, carried out jointly by the Los Angeles County Medical Association and the Tuberculosis and Health Association, indicated that almost ten thousand persons have been advised by their physicians to consider leaving the area because of the health hazards of community air pollution.

Control of motor vehicle exhaust is not the only approach to preventing air pollution of the kind that affects health. Controls for industrial emission are well developed in Los Angeles and are also being applied by local control districts in other parts of the state, in many cases with the advice and support of local health departments and medical societies. The control of incineration remains a matter of serious concern but incineration of garbage and other wastes is, except for the air pollution it causes, one of the more attractive ways of disposal. In the absence of this method additional steps are needed to manage the larger volume of material. Thus the air pollution problem is linked with the problem of disposal of garbage and of agricultural and industrial waste as well.

Another contributor to community air pollution is the combustion of fuel in power plants and for household heating. In other parts of the world, particularly London, the use of soft coal produces large amounts of particulate matter and some sulfuric acid and sulfur dioxide which are the major elements in the air pollution problem in the United Kingdom and in many other countries.

In California the major problems of air pollution from power plants derive from the combustion of sulfur-containing fuel oil, the effluents of which

tend to affect the areas downwind of the power plants. This is particularly a problem where the area downwind is residential.

Not only human health but also crops and ornamental plants are affected by air pollution. In the Los Angeles area it is no longer possible to grow lettuce, spinach, certain types of beans and tomatoes because these crops are badly damaged by the concentrations of air pollution that occur there. In some parts of the state alfalfa can no longer be grown, and there is accumulating evidence that photochemical pollution has a harmful effect on citrus fruit trees.

Concern about plant damage arises for several reasons. If the quality of the crop is impaired by air pollution, the food supply is diminished. Some of the biochemical pathways of vegetation damage are similar to those of damage to humans and other animal species; hence, insight into the biochemistry of air pollution reactions is helped by the study of vegetation damage. Economic loss through inability to grow certain types of crops in urban areas is considerable.

Among the many problems that air pollution poses for practicing physicians is how to prevent or treat the reactions observed in patients. Reactions are particularly likely to occur in persons with chronic respiratory conditions. The use of bronchodilating drugs may successfully counter the airway's reaction to inhaled irritants. Such drugs do not interfere with the perception of irritation nor with eye irritation.

It is possible to remove the irritants by filtering the air supply of hospitals, homes and automobiles through activated charcoal filters. These filters absorb and remove oxidants and ozone.

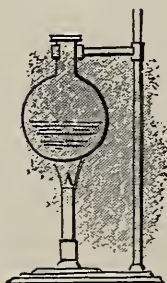
Some physicians may not be aware of an additional effect of air pollution, since their patients do not complain of it. This is the effect of carbon monoxide pollution on increasing carbonxyhemoglobin, which interferes with the oxygen transport function of the blood. In certain parts of the state there has been enough carbon monoxide in the air to inactivate 5 per cent of the circulating hemoglobin. This will affect most persons adversely and poses a special threat to those with vascular disease.

Such pollution generally occurs during the winter months when it is important to be particularly attentive to oxygenation of patients who have vascular accidents or who are recovering from surgical operation. Additional oxygen in the air supply will speed up the release of carbon monoxide combined with hemoglobin.

Control of emissions at their source remains the most dependable measure for preventing damage to health from air pollution, and the understanding and support of physicians in this effort is of great importance.

The State Department of Public Health has been asked by many persons who plan to move to California, or who are already living here, where they might move in order to avoid the health hazards of community air pollution. Such requests also, no doubt, come to physicians.

While we must respond to these inquiries, and of course we will do so, it will be an admission of inadequacy if we are unable to make all of our cities in our state a place where people can live in health and security. It is a major goal of the department to continue its studies and other efforts toward air pollution control.



Plan to Attend

CALIFORNIA MEDICAL ASSOCIATION

1968 ANNUAL SCIENTIFIC ASSEMBLY

*Fairmont and Mark Hopkins Hotels,
San Francisco, March 23-27*

EIGHTEEN SCIENTIFIC SECTION PROGRAMS ON A VARIETY OF
TOPICS PLUS FOUR GENERAL MEETINGS ON THE SUBJECTS:

- THE MANY PROBLEMS OF BLOOD
- NEW DRUG THERAPY AND REACTIONS
- TRAUMA: PREVENTION, CAUSES, TREATMENT
- PSYCHEDELIC DRUGS

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PLANS FOR THE 1968 ANNUAL SCIENTIFIC ASSEMBLY ARE NOW IN PROGRESS

PLAN **YOUR** CONTRIBUTION TO THE PROGRAM **TODAY**



WOMAN'S AUXILIARY

to the California Medical Association

Rx for Progress

**"The Secret of Success is Constancy
of Purpose."**

—Benjamin Disraeli

TO KEEP THE MEMBERS of the Woman's Auxiliary to the California Medical Association the well informed group they are noted for being, it is necessary to keep them in constant touch with the world that is changing so rapidly around them.

Program is one means of doing this. Program, for the Auxiliary, means a well integrated look at the overall activities of the organization. Some activities are stressed very much one year, not so much the next. Legislation is an excellent example of this. Being ambassadors to the public for the medical profession, physicians' wives must be as well informed as possible on every front where the medical profession may wish to carry its word.

There is a constancy of purpose in our efforts. We have tried over the years to create a public image of hardworking, dedicated women who are ever willing to espouse a cause in the interest of the public welfare.

A look at some of our efforts shows:

- AMA-ERF—largest donation from a single state Auxiliary each of the past three years.
- International Health Activities—thousands of pounds of surplus drugs and medical equipment collected and shipped to distressed areas throughout the world.

- Health Careers—hundreds of young people encouraged to enter health careers, scholarships being offered in many instances.

- Community Service—physicians' wives are not lagging in any area. Safety and Public Health (which includes Mental Health and School Health) are community problems which draw our attention more and more. Our GEMS (Good Emergency Mother Substitutes) program is very well known and appreciated by parents. A very active interest in Legislation, State and National as well as local, has been generated in recent years.

All of these efforts have a singleness of purpose—betterment of our environment.

The function of Program in this myriad of activities is to act as a coordinator, to encourage the local groups to place emphasis where it is most needed and will do the most good in their particular community.

Our State President, Mrs. William R. Flood, has given us a Prescription for Progress, the ingredients of which are Information, Imagination and Inspiration. All of these are necessary to fulfill the objectives of the Auxiliary, which are, simply, to extend the aims of the medical profession and to cultivate friendly relations among our own members. By using these ingredients, the Auxiliary can appeal to the varied interests of its members and provide them with a stimulating and challenging year.

By interesting the members, we gain in strength, and a group of 9,000 women all interested in the same goals is a cogent force. Thus is progress made. It goes hand in hand with success.

MRS. H. L. JOSEPH
2nd Vice President, WACMA
Program Chairman

LETTERS *to the Editor*

I'M GREATLY DISTURBED by your publication of the article, Marijuana: Social Benefit or Social Detriment? by Edward Bloomquist [Calif. Med., 106:346-353, May 1967]. At a time when communities all over the State are in a panic over the use of marijuana by young people, and doctors are constantly asked for advice by frightened parents, we could have wished for a solid factual article on this drug, rather than an emotional polemic.

The article is billed as a summary of contemporary thought concerning the use of marijuana. It is not. It contains many unsupported statements made in fear-inducing terms about the dangers of this drug's use. The derisive and derogatory terms used to describe drug users are designed to prejudice the reader, not to enlighten him.

More serious than the emotional bias are the errors in fact. The author refers to Goodman and Gilman as to the characteristics of the marijuana user "... sexually maladjusted (often homosexual) ... often psychopathic." It is hard to understand why an anesthesiologist would quote from a 1955 edition of a pharmacology text instead of the latest edition published in 1965. One reason might be that this inaccurate statement is omitted from the 1965 edition. However since Dr. Bloomquist has referred to the authority of the 1955 edition, you might be interested to know the lines *immediately* preceding his quote were, "... And no positive relation could be found between violent crime and the use of the drug. Marihuana is no more an aphrodisiac than is alcohol, and the drug apparently is not used for sexual stimulation. No cases of murder or sexual crimes due to marijuana were established, and Schonfield concluded that the smoking of marihuana was not associated

with juvenile delinquency. Marihuana habituation does not lead to the use of morphine, heroin, cocaine, or alcohol, and the associated use of marihuana and narcotic drugs is rare. Indeed, strong alcoholic beverages counteract the psychic effects of marihuana and are avoided by the habitue." His remarks about the LaGuardia or Mayor's Committee Report published in 1944 are totally inaccurate. I can only conclude that he has not read it. The study was not confined "to the behavior patterns and remarks of 77 prisoners." This study carried out over the period of over two years was a well constructed and detailed study of all aspects of the drug. It was designed and carried out by an illustrious panel of members of the New York Academy of Medicine, with the assistance of many other agencies in New York including the New York Police Department. It covered the chemistry and the pharmacologic, psychologic, and sociologic aspects of marijuana use. The study of the prisoners was just one portion and is a classic work on drug effects in humans. An additional portion was the study of drug users (not prisoners) in their natural habitat by specially trained police officers who lived among the users for an extended period of time observing their behavior. There has been no study made which refutes its conclusions. I believe that the widespread use of marijuana does constitute a problem—a problem which will not be solved by exaggerating the harmful effects of the drug or calling out for increasing penalties and stricter law enforcement. Dr. Bloomquist refers to the LaGuardia report as the "magna charta of the weedheads." At a time in this country when a man can be put to death for a second offense of selling marijuana to someone under the

age of 25, when mere possession of this drug can get you ten years in prison (six years in California), marijuana users need a magna charta.

The thing that most concerns me, is that this article will uncritically be accepted by physicians in this state and will be used as a basis for their remarks to patients, parents, adult groups, and young people. The result will be to increase the already high level of panic in the adults and turn off the kids. The kids will know we are lying about marijuana and will be deaf to our advice about LSD. CALIFORNIA MEDICINE owes its readers an

apology. I would hope it would take the form of an authoritative and objective article on this subject.

WILLIAM B. WENNER, M.D.
Monterey

REFERENCES

1. Goodman, Louis S., and Gilman, Alfred: *The Pharmacological Basis of Therapeutics*, 2nd Ed., MacMillan Co., New York, 1955, pp. 170-174.
2. *Ibid*, 3rd Ed., 1965, pp. 299-300.
3. Mayor's Committee on Marijuana. *The marijuana problem in the city of New York*. Lancaster, Pa. 1945, pp. 1-220, (can be found in slightly abridged form in the *Marihuana Papers*, pp. 231-353, Bobbs-Merrill 1966).

DR. WENNER'S LETTER expresses one point of view.

It should be noted that the article referred to and others of that nature were published as implementation of a California Medical Association House of Delegates resolution to inform the laity as well as the profession of the dangers of marijuana, LSD and other dangerous substances, particularly in what might be termed the drug-dependent-prone individual.

The articles were intended to be informative in pointing up the hazards and dangers rather than the presumed delights of these substances.

Parachute jumping presumably appears to be a pleasant and safe hobby to the parachute jumper and he naturally somewhat ignores the consequences should his chute fail to open.

The point here, then, was to emphasize the calculated risks with a hard rather than a soft sell.

Dr. Wenner is entitled to his opinions but these are also somewhat speculative.

There are 2,300 former hardcore addicts in the rehabilitation program at Corona. Practically all

of them stated that they started on marijuana and graduated to heroin. Most of them agreed that without the permissive attitude induced by marijuana, they felt they would not have tried heroin.

It is estimated that a million people in the United States have tried marijuana and it is generally conceded that 5 to 10 per cent go on to heroin addiction. It is hard, therefore, to rationalize legislation which would make its use comparable to alcohol. One headache doesn't justify another headache.

The United Nations Narcotic Bulletin contains many documented examples of crimes of violence under the influence of marijuana.

It would, therefore, seem in the interest of the public and the profession, that the hazards and dangers be emphasized, even while well recognizing that there may be others sincerely more permissive in their approach in this as in many other matters of concern to the profession.

WILLIAM F. QUINN, M.D., *Chairman*
CMA Committee on Drugs
Chairman, California State Narcotics
Advisory Commission

NEWS & NOTES

NATIONAL • STATE • COUNTY

LOS ANGELES

The Childrens Hospital of Los Angeles will hold its sixth clinical **conference in pediatric anesthesiology** 26 to 28 January 1968.

Additional information may be obtained from Dr. Wayne Herbert, Childrens Hospital of Los Angeles, 4650 Sunset Boulevard, Los Angeles 90027.

SAN FRANCISCO

Dr. Roberta Fenlon of San Francisco received a Distinguished Achievement Citation at an Alumni Day meeting of Iowa State University last month. The citation is given in recognition of outstanding professional achievement. Dr. Fenlon, who received an M.S. degree at Iowa State and her doctorate in medicine at the University of Iowa, is a member of the Council of the California Medical Association. She is in private practice in San Francisco and is also a member of the faculty at University of California School of Medicine there.

SANTA CLARA

Dr. Robert J. Glaser, vice-president for medical affairs and dean of the Stanford University School of Medicine, has been appointed to a 15-member **national advisory committee on higher education** to explore the relationship between colleges, universities and the federal government.

The committee was appointed by John W. Gardner, Secretary of Health, Education, and Welfare. "The growing partnership between the federal government and the universities must be a relationship in which neither side exploits the other," Secretary Gardner said. "If we are to reap the benefits and avoid the dangers in the relationship, we shall have to understand it far better than we do now."

The committee will examine the present quality of relationships between higher education and HEW. The overall relationships of colleges and universities with the federal government also will be reviewed. The committee will identify problems and make proposals for their solution.

Before coming to Stanford, Dr. Glaser was president of Affiliated Hospitals Center, Inc. and professor of social medicine at Harvard Medical School.

GENERAL

The Society for Investigative Dermatology named **Dr. Marion B. Sulzberger** of San Francisco as the first recipient of an annual award to honor those who have "distinctly altered the course and image of dermatology."

The award—named after Dr. Stephen Rothman, one of the society's early leaders—was given at the annual meeting of the organization held recently in Atlantic City. The award consists of a gold plaque bearing the likeness of Dr. Rothman, and a \$1,000 honorarium.

Dr. Eugene M. Farber of Palo Alto, president of the society, and Head of the Department of Dermatology at the University of California at San Francisco, presented the award.

At the same meeting, the appointment of **Dr. Richard E. Stoughton** of La Jolla as editor of the *Journal of Investigative Dermatology* was announced. Dr. Stoughton is director of the Division of Dermatology at the Scripps Clinic. He succeeds Dr. Naomi M. Kanof of Washington, D.C., as editor.

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The American College of Gastroenterology announces that its annual course in postgraduate gastroenterology will be given at The Biltmore Hotel in Los Angeles, 2 to 4 November 1967.

Further information may be obtained from the American College of Gastroenterology, 33 West 60th Street, New York, N.Y. 10023.

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The ninth national **Conference on the Medical Aspects of Sports**, sponsored by the American Medical Association under the auspices of its Committee on the Medical Aspects of Sports, will be held in Houston 26 November 1967, the first day of the Clinical Convention of the American Medical Association.

The conference will cover a wide range of subjects of interest to those serving school and college athletic programs. Included will be forums and discussion sections relating to prevention of knee injuries, sports cardiology, and quackery in sports. Two sessions will be devoted to a series of common clinical conditions of rather variable significance in the athletic setting.

The conference is open to key nonmedical athletic personnel as well as to interested physicians. Further information may be obtained from the Committee on the Medical Aspects of Sports, American Medical Association, 535 North Dearborn Street, Chicago 60610.



The Physician's BOOKSHELF

PRINCIPLES OF INTERNAL MEDICINE—Fifth Ed.—
Editors: T. H. Harrison, A.B., M.D., M.S. (Hon.), D.Sc. (Hon.), Professor of Medicine, The Medical College of the University of Alabama, Distinguished Professor, University of Alabama, Birmingham; Raymond D. Adams, B.A., M.A., M.D., M.A. (Hon.), Bullard Professor of Neuropathology, Harvard Medical School, Boston; Ivan L. Bennett, Jr., A.B., M.D., Baxley Professor of Pathology and Director of the Department of Pathology, Johns Hopkins University School of Medicine, Baltimore; William H. Resnik, Ph.B., M.D., Clinical Professor of Medicine, Yale University School of Medicine, New Haven; George W. Thorn, M.D., M.A. (Hon.), LL.D. (Hon.), Sc.D. (Hon.), Hersey Professor of the Theory and Practice of Physic, Harvard Medical School, Physician-in-Chief, Peter Bent Brigham Hospital, Boston; and M. M. Wintrobe, B.A., M.D., B.Sc. (Med.), Ph.D., D.Sc. (Hon.), Professor and Head, Department of Medicine, and Director, Laboratory for Study of Hereditary and Metabolic Disorders, University of Utah College of Medicine, Salt Lake City. McGraw-Hill Book Company (The Blakiston Division), New York, 1966. 1,874 pages, \$22.50.

In their fifth edition of *Principles of Internal Medicine* the editors maintain the high standard they established when this textbook was first offered in 1950. The present volume has a total of 1874 pages, including a very adequate index and chapter bibliographies, which are largely limited to reviews and monographs. In arranging the book, the editors have tried to recapitulate the steps in the process of thinking by which a physician reaches a diagnosis: The interpretation of the patient's symptoms, the recognition of a constellation of symptoms and finally a consideration of the various disorders which could cause the clinical picture.

There is something in this book for all physicians. In using it, the experienced physician may turn directly to the disease with which he is concerned. The medical student should read through the chapters on cardinal manifestation of disease and the introductory chapters on common syndrome. And any house officer or practitioner confronted with a diagnostic problem or an unfamiliar group of signs and symptoms will find all the discussions helpful.

The individual sections and chapters are too numerous and diverse to comment on in a short book review. But one can summarize succinctly: Fully recommended!

EDGAR WAYBURN, M.D.

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RENAL CARCINOMA—By James L. Bennington, M.D., Director of Pathology, King County Hospital, Seattle; and Assistant Professor of Pathology, University of Washington, School of Medicine; and Robert M. Kradjian, M.D., Staff Surgeon, Kaiser Foundation Hospital, Oakland, California; Consulting Surgeon, Highland Alameda Hospital, Oakland. W. B. Saunders Company, West Washington Square, Philadelphia, Pa. 19105, 1967. 263 pages, illustrated, \$15.00.

The writing of this monograph on *Renal Carcinoma* was prompted, according to the authors, Bennington and Kradjian, by "personal frustration in trying to obtain

reliable sources of information on various aspects of this disease." The book was intended to provide a comprehensive review of all the significant knowledge about renal carcinoma and as an atlas of its morphologic characteristics. The authors have succeeded admirably, with a thorough discussion of the embryology and anatomy of the kidney, and the histogenesis, epidemiology, etiology and experimental production of renal cancer, including its morphology, distribution of metastases, signs and symptoms, diagnostic techniques, treatment and prognosis. The text is clearly written and the illustrations, which are plentiful, well-chosen and generally excellent, include a number of electron photomicrographs. A very extensive bibliography on all aspects of renal carcinoma is included. This well-conceived monograph should be of considerable interest and value to many physicians and surgeons as well as pathologists. Some readers, however, may have the same reaction as the small boy who returned a very large book on alligators to the library after only one day. When asked by the librarian why he had returned the book so soon, he replied, "I really didn't want to know that much about alligators."

STUART LINDSAY, M.D.

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PATHOLOGY ANNUAL, Volume 2, 1967—Series Editor, Sheldon C. Sommers, M.D., Professor of Pathology, Columbia University College of Physicians and Surgeons; Associate Director of Laboratories, Francis Delafield Hospital, New York, New York; Clinical Professor of Pathology, University of Southern California School of Medicine, Los Angeles, California. Appleton-Century-Crofts (Division of Meredith Publishing Company), 440 Park Ave., So., New York, N.Y. 10016, 1967. 427 pages, \$13.75.

This volume is the second of the *Pathology Annual Series* edited by Sheldon Sommers. The 13 essays are by distinguished pathologists on subjects that are of special interest or within the particular sphere of experience of each author. Although intended primarily for the practicing pathologist, physicians in other fields will find these expositions, covering as they do many fields of medicine, well worth reading.

Included in the annual are essays on sarcoidosis, carcinoma-in-situ of the breast, recent research on prostatic pathology, dietary aspects of atherosclerosis, renal tumors, significance of extracellular hyaline substances, and nevi and melanomas. Especially outstanding papers, in the opinion of this reviewer, are those by McGovern on "Glomerulonephritis," by Lev on "Transposition of the Arterial Trunks in Levocardia," by Angrist, Oka and Nakao on "Vegetative Endocarditis," by Edmondson and Peters on "Diagnostic Problems in Liver Biopsies," by Berg on "Intersections of Epidemiology and Biostatistics with Pathology," and by Russfield on "Pituitary Tumors." The last chapter is a delightful minor tragedy in 12 scenes by Foraker entitled "A Day in the Life of a Hos-

pital Pathologist," which should appeal mainly to masochistic pathologists.

This volume is well illustrated and the photographs are almost uniformly excellent. These reviews are timely and make a welcome addition to pathology literature. It is hoped that this series will continue to appear for a long time to come.

STUART LINDSAY, M.D.

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METABOLIC TOXEMIA OF LATE PREGNANCY—A Disease of Malnutrition—By Thomas H. Brewer, M.D., County Physician, Richmond Health Center, Richmond, Calif.; formerly, Instructor, Department of Obstetrics-Gynecology, University of California Medical Center, San Francisco, Calif. Charles C Thomas, Publisher, Springfield, Ill., 1966. 127 pages, \$8.50.

This is an interesting volume in which the author puts forth his ideas concerning the etiology of toxemia of pregnancy. To quote from the first page of the introduction: "Scientific evidence will be presented which clearly indicates that toxemia of late pregnancy is a disease of nutritional deficiency mediated through hepatic dysfunction and that the bacterial flora of the maternal gastrointestinal tract, as well as the steroid hormones (estrogens and progesterone) produced by the placenta, play a contributing role in its pathogenesis." He presents some of his own extensive experience as well as selected references from the literature to support his thesis.

He suggests that malnutrition is the basic cause of toxemia and that it results in hepatic lesions and dysfunction. In support of this hypothesis, he cites pathologic lesions found by Maqueo and states that in these women, a direct correlation was found between a history of low protein intake and the severity of toxemia. Other authors, of course, have reported great variability in the extent and severity of the hepatic lesions, and have found no lesions at all in some patients in whom the disease was so severe that the patients had eclampsia.

He emphasizes the importance of hypoalbuminemia in lowering oncotic pressure, thus permitting tissue edema, but states that the cause of hypoalbuminemia in metabolic toxemia of late pregnancy is not known at present. He does recommend the use of intravenous albumin instead of diuretics.

Some comments are made about the diminished conjugation of placental steroids, and the suggestion is made that the toxemic woman is actually overloaded with placental steroids. The author suspects that sodium-retaining steroids play an important role in the sodium and water retention seen in women who develop clinical edema in pregnancy.

These remarks concerning placental steroids are much too simple and naive. We need much more information about plasma levels, production rates, and details of metabolism of these steroids before any meaningful comments can be made.

The suggestion is made that certain aromatic amino acids are affected by the bacteria of the lower gastrointestinal tract with the production of compounds which may accumulate within hepatic cells and damage or destroy those cells. Ten patients who were treated with neomycin in order to prevent this reaction are presented along with three similar patients who did not receive neomycin. The author feels that loss of edema as determined by loss of weight was quite clearly related to the use of neomycin but many of the patients were started on treatment soon after hospitalization, and it is quite possible that the bed rest contributed heavily to the weight loss. For example, his third "control" patient lost

weight without receiving neomycin. Most of these patients had quite mild examples of toxemia and there is no clear relationship between improvement in the toxemia and neomycin therapy.

A very nice section is included concerning the prevention of toxemia through prenatal nutritional education. Doctor Brewer correctly emphasizes the importance of stressing the value of good nutrition to prenatal patients, and the necessity of reviewing the matter at subsequent prenatal visits. His experience has been quite gratifying in that of the first 235 patients who have delivered, there has not been a single case of metabolic toxemia of late pregnancy.

In summary, I found this to be a very interesting essay concerning the author's hypothesis of the etiology of toxemia of pregnancy. I do not consider the hypothesis well proved from the evidence presented here, but many thought provoking suggestions are made. The emphasis on good nutritional guidance for prenatal patients is very well taken.

WILLIAM J. DIGNAM, M.D.

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HUANG TI NEI CHING SU WEN—The Yellow Emperor's Classic of Internal Medicine—By Ilza Veith. University of California Press, Berkeley and Los Angeles, 1966. 260 pages, \$8.00.

It is indeed a pleasure to welcome back into the fold of the "available" this great classic of Chinese medicine, the *Nei Ching*. It has for too long been "out of print," which is unfortunate since it is the single most important work in English for the understanding of the basis of traditional Chinese medicine. It should not be forgotten that perhaps today more people are treated for their ills on the archaic principles (or some modification of them) discussed in this text than are reached by modern Western medicine. Oddly enough, and to some extent initiated by political considerations, there has been a curious and recent resurgence of these ancient methods of therapy, not only in China itself but all over Europe—notably in Russia, France, and Great Britain—which has begun to extend to the United States. Medical journals devoted exclusively to treatment by acupuncture, moxibustion, and other methods based on such antiquated theories, are presently being published in France and the United Kingdom, and possibly elsewhere in the West. Consequently Dr. Veith's book is, in the context of the present day, a good deal more than a significant achievement in the history of medicine. It has become an important social document for the understanding of existing socio-political conditions in the Far East and the irrational aberrations of the West.

The *Nei Ching* is reputed to be the oldest medical text in existence, but this should be accepted with a great deal of caution since legend and reality are so hopelessly intertwined as to make dating impossible. The authorship is ascribed to Huang Ti (the Yellow Emperor), said to be the third of China's first five rulers who flourished circa 2697-2597 B.C. but whose very existence is problematical. Nonetheless, Huang Ti is venerated and worshiped as the father of Chinese Medicine. The existing text is apparently a reworking of an earlier version completed about 762 A.D., but which was certainly in existence during the Han dynasty (circa 206 B.C.-25 A.D.). Doubtless it has passed through many recensions by commentators over hundreds of years, so that little of the original remains. The *Nei Ching* is an immense work, and this volume is the first

and only translation of a major part of it into a Western tongue.

Dr. Veith's translation is accompanied by a most extensive and important introduction which makes the complex philosophical basis and medical system comprehensible. This introduction is by far the most readable, enlightening, and clear account in the literature. This classic is a work of the greatest significance for the general reader interested in sinological matters as well as for physicians, particularly those in California who not infrequently encounter the results of traditional medicine in the state's large Chinese and Japanese population. But even more important, it provides insight into the nature of the Chinese civilization and an aspect of the modern problems of that civilization.

Finally, this is a beautiful book, somewhat smaller in format than the original edition and a reprint of high quality. Unfortunately, not all of the typographical errors from the earlier edition have been corrected.

J. B. DE C. M. SAUNDERS, M.D.

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PULMONARY DISEASES AND ANOMALIES OF INFANCY AND CHILDHOOD—Their Diagnosis and Treatment—By Milton I. Levine, M.D., F.A.C.C.P., Attending Pediatrician, New York Hospital; Associate Professor of Clinical Pediatrics, Cornell University Medical Center; Director, Pediatric Pulmonary Clinic, New York Hospital, New York City; and Armond V. Mascia, M.D., F.A.C.C.P., Assistant Attending Pediatrician, New York Hospital; Assistant Professor of Clinical Pediatrics, Cornell University Medical College; Member, Pediatric Pulmonary Clinic, New York Hospital, New York City; Director, Pediatrics, Phelps Memorial Hospital, Tarrytown, New York. Hoeber Medical Division, Harper & Row, Publishers, New York and London, 1966. 368 pages, \$12.00.

This volume is intended to fill a need which has long been felt by every physician who deals with diseases of the chest. No book of this scope has been published previously in the English language. Textbooks relating to chest diseases in adults have neglected to give adequate coverage to the peculiar problems of infancy and childhood. After reviewing this volume it becomes apparent that pediatric chest diseases constitutes a field so broad that it deserves a special textbook.

Physicians with a special interest in tuberculosis will find much to complain about in this book but the references cited should make up for these deficiencies. Foreign bodies in the bronchi must be more important than would be judged by the discussion given here. Many other important topics are given very brief mention with similar or greater space devoted to conditions which are rarely encountered. But the book is a very brief one and attempts to cover too broad a field in such space. Fortunately there are generous references to the literature after most chapters and the student is urged to make use of these.

The illustrations are of good quality and the book is well made. The index leaves much to be desired.

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A MANUAL OF CLINICAL ALLERGY—Second Edition—By John M. Sheldon, M.D., Professor of Internal Medicine, University of Michigan Medical School; Robert G. Lovell, M.D., Associate Professor of Internal Medicine, The University of Michigan Medical School; and Kenneth P. Mathews, M.D., Professor of Internal Medicine, University of Michigan Medical School. W. B. Saunders Company, 600 West Washington Square, Philadelphia, Pa. (19105), 1967. 550 pages, \$15.00.

In the Preface of the First Edition published fifteen years ago, the authors stated: "This book is prepared for the physician interested in devoting part of his time to the treatment of allergy patients, or in establishing

an allergy practice . . . There are a number of excellent textbooks and several journals on the subject of allergy. This manual does not attempt to replace or supplant such texts and periodicals but rather should be used in conjunction with them." The second edition continues to emphasize this objective. With exception of a first chapter of 19 pages on *Immunology and Immunochemistry of Allergy*, the book is practically devoid of theory and is concerned almost entirely with the clinical diagnosis and treatment of the more common allergy diseases.

Since the first edition was offered, a new chapter on insect hypersensitivity has been added and there have been substantial extensions of two others. All the diagnostic facets of allergy are described. Specific treatment and hyposensitization to inhalant allergens are fully discussed. Other forms of treatment are carefully evaluated. Although the authors naturally express their own opinions they are sound and are those held by the majority of practicing allergists. The drugs used in symptomatic treatment are listed and this is a valuable chapter. Although under the heading of *The Passing Parade of Medication*, the description of various proposed allergy medicines and procedures that have not proved of value is brief, it is interesting and should be enlightening to physicians who do not read the reports of the allergy drug investigating committees of the national allergy societies.

Appendix I gives a detailed account of how allergenic extracts are made. Undoubtedly, most physicians practicing part-time allergy or just entering into the specialty will prefer to purchase their allergenic extracts rather than equip a laboratory and get involved in the technical procedures of grinding, extracting, dialysing, standardizing, etcetera; nevertheless, anyone who treats allergy patients and uses these extracts should have some idea of how they are prepared.

In conclusion, this volume is a clear, concise allergy manual that should be in the library of every physician who treats allergy diseases; it will be referred to often.

M. COLEMAN HARRIS, M.D.

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MANUAL OF TROPICAL MEDICINE—Fourth Edition—By George W. Hunter, III, Ph.D., Col. U.S.A. (Ret.), Lecturer, Microbiology and Biological Sciences, College of Medicine, University of Florida, Gainesville, Florida; formerly, Resident Coordinator of LSU-ICMRT and Research Professor of Medical Parasitology, Department of Tropical Medicine and Medical Parasitology, Louisiana State University, School of Medicine, New Orleans; William W. Frye, Ph.D., M.D., Sc.D. (Hon.), Professor of Tropical Medicine, Director of LSU International Research and Training Programs in Tropical Medicine; and J. Clyde Swartzwelder, Ph.D., Professor of Medical Parasitology and Head of Department of Tropical Medicine and Medical Parasitology, Co-Director, LSU International Research and Training Programs in Tropical Medicine, Louisiana State University, School of Medicine, New Orleans. W. B. Saunders Company, Philadelphia and London, 1966. 931 pages, \$18.50.

This edition of the manual offers a fairly comprehensive presentation of tropical area diseases which are now assuming worldwide importance as travel habits become more extensive.

The manifold aspects of virus diseases in the tropics are discussed quite effectively in a style different from the conventional method of etiologic classification. The differentiation into the various clinical syndromes produced is probably a more effective concept of a complex subject caused by a wide variety of etiologic agents. Description of the epidemiology of the various arboviruses, vector variations, and geographical distribution is a useful tool to the public health worker. Recent diagnostic and therapeutic developments for parasitic diseases as well as the

therapy of resistant falciparum malaria are included. Discussion of such medical problems as cholera, dengue fever, and schistosomiasis is of renewed interest while recently recognized diseases as Kuru and Acanthamoeba infections are brought to the attention of the reader. Laboratory techniques are adequately described.

The utility of the book as a standard reference for tropical diseases both for the medical student and the practitioner is enhanced by the appendix attempting to enumerate diseases present in geographical areas of the world. Although the list is far from complete, presumably due to inadequacies of disease-reporting methods, it serves as a guide to the recognition of an illness which may have been contracted abroad and manifested only upon return to the United States.

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CLINICAL OBSTETRICS AND GYNECOLOGY—Volume 10, Number 1, March 1967—Hormones in Reproduction, edited by Robert B. Jaffe, M.D., and Female Urology, edited by Tiffany J. Williams, M.D. Published quarterly by Hoeber Medical Division, Harper & Row, Publishers, 49 East 33rd Street, New York, N.Y. 10016, about 1200 pages per year. Subscription: \$18.00 per year.

This little volume will serve as a quick summary of current thinking in two disparate fields. As such it is not intended to, nor does it, fill the need for comprehensive research or practical management.

The first portion deals briefly with various aspects of hormones related to reproduction. At times it suffers from oversimplification not all of which can be ascribed to the brevity of the discussion. Concerning the interaction of sex steroids at end organs it is of interest that protein receptors for estradiol do not bind biologically active diethylstilbesterol or progesterone. Theories of hormone action are presented in a simplified manner with which readers with some background in the field might quibble. There is no mention of Bonner's work. Useful information concerning steroid levels is given. However the discussion concerning urinary assays and significance of estriol could have been expanded. Progesterone and estrogen metabolism by the placenta receives good coverage. The section entitled "non-steroidal estrogen antagonists" is concerned with a subject which has received intense attention in recent years. Induction of ovulation represents a major clinical breakthrough. The discussion does not emphasize the necessity for a potentially responsive ovary and the means to delineate this fact. Excellent consideration of the adrenal gland and hypothalamus are given. Immunoassay of human gonadotropins receives competent coverage. However this reviewer finds it difficult to reconcile a sensitive assay procedure with the fact that assayed polypeptides share similar antigenic binding sites. Considerable restraint in interpretation of immunologic data would seem warranted at present.

The last portion (approximately 1/3) of the book dealing with female urology is well organized although portions may be oversimplified and too general to be useful. This reviewer found the discussion of antibiotic therapy informative. There is an interesting discussion of interstitial cystitis, often a cause of intractable urgency incontinence. The section describing bladder care after operation reflects the current trend away from prophylactic catheterization. The discussion concerning urinary diversion reflects vast experience and dampened enthusiasm for the procedure. Ileal conduit is simply mentioned. A section pertaining to retroperitoneal fibrosis may not be particularly useful to gynecological surgeons.

STANLEY J. GROSS, M.D.

DERMATOLOGIC ALLERGY: IMMUNOLOGY, DIAGNOSIS, MANAGEMENT—By Leo H. Crip, M.D., F.A.C.P., Clinical Associate Professor of Medicine, School of Medicine, University of Pittsburgh; Chief of Allergy, Montefiore Hospital; Director, Central Allergy Laboratory, Veterans Administration; Consultant, Medical Staff, Presbyterian-University and Magee Hospitals. With the collaboration of 15 contributors. W. B. Saunders Company, Philadelphia and London, 1967. 605 pages, \$17.00.

Recent years have seen an increasing need for a textbook in the field of cutaneous medicine which would present clearly and simply the rapidly accumulating knowledge in basic immunology and its allied specialties as it pertains to dermatology. This has been achieved to a great extent by Dr. Crip and an eminently qualified panel of contributors.

Most of the contents are devoted to the presentation of various facets of immunologic knowledge as it involves skin diseases and is particularly valuable to the student of dermatological allergy. This book represents the best attempt to present which summarizes current immunological data as it pertains to diseases of dermatological origin and from this standpoint it can be recommended as a valuable addition to one's library.

VICTOR D. NEWCOMER, M.D.

* * *

OSLER'S TEXTBOOK REVISITED—Reprint of selected sections with commentaries—Edited by A. McGehee Harvey, Professor of Medicine and Chairman, Department of Medicine, and Victor A. McKusick, Professor of Medicine, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, Appleton-Century-Crofts, New York (Division of Meredith Publishing Company), 1967. 361 pages, \$6.75 (Paperback).

Professors Harvey and McKusick of the Department of Medicine at Johns Hopkins visit the famous textbook of their distinguished predecessor, William Osler, by presenting selections from the seventh edition (1909) of *The Principles and Practice of Medicine*, the last edition to be written by the author without collaboration. To the 24 topics selected, some 17 commentaries have been appended, each written by some noted specialist. The commentaries purport to bring the reader up to date by means of a brief survey of progress since 1909, although the purpose of these sketches remains unclear. In addition, the editors provide a short introduction in which the circumstances of composition, collaborative authorship, influence, and organization of the text are discussed together with some tables on selected advances in medicine from 1875 (when Osler entered academic life) to 1892, and from 1892 (the date of the first edition) to 1909. An epilogue concludes with the observation that of all the sections visited "at the level of clinical and pathological description of the natural history of disease nothing substantial has been added since Osler's resumé of 1909. What has been added in our understanding is mainly in the realms of etiology, pathogenesis, and therapy."

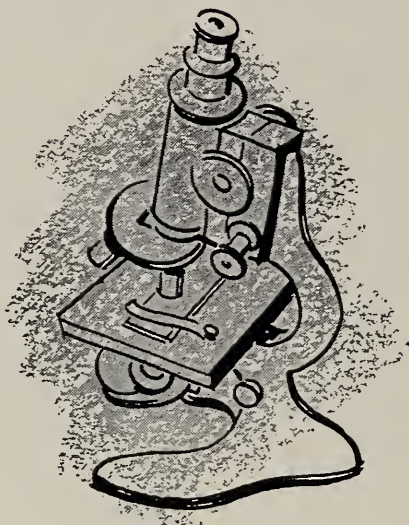
There is no doubt that William Osler's *The Principles and Practice of Medicine* was for more than a generation the most influential textbook on the North American continent. Its influence extended not only to the majority of the teachers of the present generation of American physicians but is credited with a major role in directing philanthropy, notably that of John D. Rockefeller, towards the support of research and improvement of education in medicine and public health. Although translated into French, German, Spanish and Chinese, contrary to the statements of the editors of the present work, Osler's textbook never achieved the same popularity abroad. As Henry Sigerist, the distinguished medi-

cal historian at John Hopkins, wrote more than a generation ago when Osler's influence was very real, "The physicians of the European continent do not know much about him. The older ones have heard of him as a clinician. . . . To the younger men he is almost unknown." In the British Isles, Osler's textbook was not popular, and in Germany it was no rival to Ernst Strümpell's parallel book first published in 1883, which was likewise translated into a number of foreign languages. Consequently, Sigerist was compelled to observe that it was not as a discoverer or in his literary work that Osler cast a spell on posterity. "The secret of Osler's influence must be looked for elsewhere. It lies in his personality, in his inimitable qualities as a physician, a teacher, and a man." Sigerist concluded that the textbook belongs to the literary deposition of a great age in medicine which with

Strümpell's book "will one day be recognized as sources of important historical material."

The failure to recognize Sigerist's admonition has made the revisit to Osler's distinguished textbook so unsatisfactory and disappointing. A great opportunity has been lost in the failure to present the work in its true contemporary context or to watch progress unfold through the changing image reflected by a textbook which has had a run of more than half a century. But the disappointment is ameliorated with the recognition that this "paperback" selection may serve to place in the hands of students a convenient access to those values in clinical medicine which are too often forgotten in current teaching.

JOHN B. DEC. M. SAUNDERS, M.D.



MEDICAL STAFF CONFERENCE

Current Status of Renal Homotransplantation

These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California Medical Center, San Francisco. Taken from transcriptions, they are prepared by Drs. Martin J. Cline and Hibbard E. Williams, Assistant Professors of Medicine, under the direction of Dr. Lloyd H. Smith, Jr., Professor of Medicine and Chairman of the Department of Medicine.

DR. LLOYD H. SMITH, JR.*¹: I think we would all agree that there are few areas in medicine in which there have been more dramatic and rewarding advances over the past few years than in homotransplantation. We can also say that it is an area of medical activity which illustrates *par excellence* the importance of very close cooperation between all of the medical disciplines. This cooperation, particularly between the Departments of Surgery and Medicine, is reflected in the superb results that have been achieved in this hospital. It represents success that has been won with great difficulties. I think this point will be illustrated in the presentations that will be given today.

The program this morning is under the direction of Drs. John Najarian and Paul Gulyassy. They have taken a leading part in the developments which will be discussed. I might point out that a recent, almost semi-popular book written about this subject was entitled *Give and Take*¹ and I hope that during the presentations today this will be somewhat of an aphorism that we can apply for

educational purposes. I would like to turn the program over to Dr. John Najarian.

DR. JOHN S. NAJARIAN*²: Last year we talked about the history of tissue transplantation and discussed the present status of kidney transplants. This morning we should like once more to bring our material up to date and delineate the horizons of transplantations. We shall point out the stumbling-blocks and some of the problems that we have overcome. I think it well to preface our remarks by indicating the areas of major interest and possible improvements that can be made in the results of tissue transplantation. Specifically, we shall be talking about renal homotransplants. I should like to point out that kidney transplantation is a very definite therapeutic measure that can be used in patients with end-stage kidney disease, although the scope of its application is still limited. I think that all who have participated in our own program would agree. The important thing is that now this particular tool is available, we must

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*²Professor and Vice Chairman; Chief, Transplant Service, Department of Surgery.

define more clearly some of the obscure changes occurring in our patients and their transplanted kidneys. We must ask how we can improve our results.

Of major interest to those actively engaged in transplantations is histocompatibility typing. In the steadily enlarging field of transplantation, people are constantly trying to find better ways to obtain genetic matching. We can summarize what has happened in this regard across the country (Chart 1). The chart is taken from the National Kidney Registry at Boston and summarizes data through 1964. It is well to remember that the number of transplants performed up to the year 1961 was 56, most of them in identical twins. There was some interest in renal transplantation in 1961, which increased greatly in the latter part of 1962 and the method became firmly established in 1963 with the advent of immunosuppressive drugs. We are now in the phase of immunosuppressive drug therapy and there has been an almost exponential rise in the number of transplants performed in this country and abroad. Although the Registry figures are not up to date, it has been estimated that approximately a thousand renal homotransplants have been performed in patients who were not identical twins. You will notice that the over-all survival rate continues to improve; it was between 38 per cent and 48 per cent in 1964, and in 1965 it was slightly higher.

Let us focus on the problems that are now before us. The first is genetic matching methods for donor selection. Because of limited funds and facilities we have not applied these procedures, but instead have concentrated our efforts on consanguineous or blood-related donors. We have transplanted kidney grafts from unrelated donors and have performed one graft with a cadaver donor. However, we are quite interested in methods for obtaining a better genetic match between donor and recipient. I have listed four possible tests (Table 1) but there is also a fifth test. The first method is the triple skin graft. This technique, developed initially in Boston, has been more or less abandoned. It involved using a volunteer who

became a third-party for a skin graft from the recipient and eventually from the prospective donor; accelerated rejection of the skin graft indicated some degree of genetic similarity—a very crude test which did not prove to be worthwhile.

The second test was based on a delayed sensitivity skin reaction; peripheral leukocytes were obtained from the recipient and then were injected beneath the skin of the donor. The amount of reaction was supposed to reflect the genetic similarity between the donor and recipient. Again, this method was unsatisfactory for many reasons.

The third test involved lymphocyte transformation. We all thought at first that this was the answer; this technique, proposed by Bains and Hirschhorn,² was based on the transformation of lymphocytes *in vitro*, which depended upon the genetic dissimilarity between cells of the graft donor and recipient. The degree of transformation was directly related to the genetic difference between the individuals. Unfortunately, it has subsequently been found that cells from uremic patients do not respond in the same way as do those from normal people.

The fourth test involves antilymphocytic antibody and we will discuss this at length later in the presentation. Dr. Paul I. Terasaki and Dr. Roy L. Walford at UCLA have used this particular method as a matching technique. They obtain leukocyte cells from the prospective recipient and the prospective donor and test them against a large spectrum of antiserum obtained from 150 persons, against lymphocytes. The degree of matching between these lymphocytes is indicated by the number of tubes that are similar in the degree of cytolysis caused by a particular antilymphocytic serum. This has proven to be a fairly worthwhile test, but cumbersome.

TABLE 1.—Genetic Matching Procedures For Donor Selection

1. Triple skin graft
2. Delayed sensitivity skin reaction (Brent)
3. Lymphocyte transformation (Hirschhorn)
4. Antilymphocytic antibody (Terasaki)

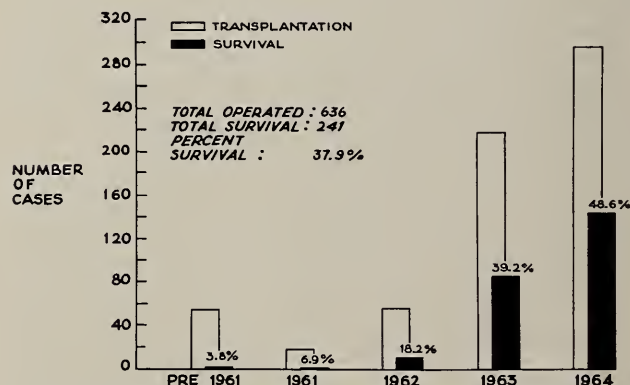


Chart 1.—Renal homotransplantation survival distribution (excluding monozygotic twins). Kidney Transplant Registry, 15 March 1965.

We have been engaged in a retrospective study in which our own results were correlated with leukocyte agglutination tests. This is a method of typing leukocytes developed by Dr. Herbert Perkins (U.C. Medical Center) and by Dr. Rose Payne (Stanford Medical Center). The results are still incomplete. We hope that eventually we can type leukocytes as well as red cells and that with proper leukocyte type-matches we shall find good genetic donor combinations.

I would like to stress that all these techniques would involve the use of unrelated donors or cadaver kidneys. We need better methods of organ preservation before these donors are really practical.

The second major area we shall discuss today is that of immunosuppressive drugs. The agents currently available are rather crude. In essence they are like large mallets where a rather small hammer is needed. We are looking for more specific methods of immunosuppression.

The third problem that we shall discuss is that of early renal failure. Chart 2 is taken from Benjamin Barnes' analysis of the data from the Kidney Registry.³ On the top line are listed identical twins. We see that they have survived for some eight years and that about two-thirds of all the identical twins that were operated upon are still living and have functioning kidneys. From these data we can also extrapolate what happens to sibling donors. We see that there is a very pronounced rate of early attrition; deaths from early failure usually occur within the first two months, then there is a leveling off period. The rate of attrition of these patients is minimal after the first year.

The problems to which we have addressed ourselves are: (1) what is the cause of this early attrition, and (2) can we find some means of treating

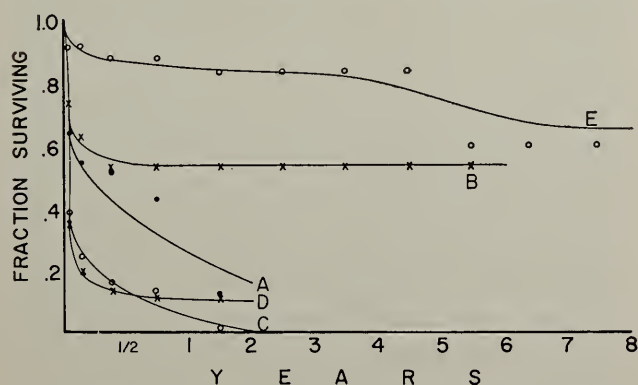


Chart 2.—Survival of renal homotransplants when donor source was a parent (line A); a sibling (B); unrelated (C); a cadaver (D); a monozygotic twin (E).

early renal failure or at least of making the results closely resemble those obtained with identical twins. Dr. Gulyassy will discuss this in detail in just a moment.

Today we would like to discuss how we select our donors and recipients, how we prepare our recipients for transplantation, the drugs we currently use for immunosuppression, and perhaps in a crystal-ball fashion try to envision techniques of better immunosuppression. We will then talk about rejection. We shall present several patients and will try to allow enough time for discussion. Dr. Gulyassy will now talk about the selection of the donor-recipient and the preparation of the recipient.

DR. PAUL F. GULYASSY*³: Before we consider how we evaluate both the recipient and the donor for transplantation, I would like to emphasize the following point: Although we do not make the decision to proceed with homotransplantation until the potential recipient has clearly reached the end stage of renal disease and rigid medical management can no longer safely maintain the patient, we would like to evaluate potential recipients long before this time is reached. The reason is that we must go through a very complex, time-consuming series of evaluations of both the recipient and potential donors. In addition, the ultimate deterioration of the patient who has had chronic renal disease for some time is totally unpredictable. We are in a poor position to evaluate and prepare the patient with chronic uremia if his disease has been allowed to progress to the point of convulsion and coma. We urge that any potential recipients be called to our attention when the patient has moderately advanced, but not terminal uremia.

In considering the potential recipient the major criteria which we evaluate are as follows. First, the patient as stated must have irreversible and advanced renal failure. The usual methods are used to prove that the problem is not one of acute or subacute renal disease, and only after all attempts have been made with medical management to produce reversal of symptoms and abnormalities will we consider the patient for more definitive therapy. Second, we must be sure that the patient does not have irreversible, advanced systemic disease of such a nature that even with a successful, perfectly functioning graft he is liable to die anyway. We have done transplantations in patients with minor systemic defects when the particular

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disease was stable and would not be affected by surgical or drug therapy. Third, obviously a suitable donor must be available and in our experience we have so far used mainly consanguinous, living donors. We will consider any patients between approximately 10 and 50 years of age. Below or above these age limits, we will consider only very carefully selected patients. Finally because of the very extensive and trying experience which both the preoperative and postoperative course entails, we must have patients who are free of any major psychiatric disorders.

Let us consider the donor. When we are using living, consanguinous donors, we must do an exhaustive evaluation of the donor for two reasons: First, to insure that he has a normal kidney and genito-urinary tract; and second, that the major operation of nephrectomy will be safe for him. Therefore, we perform a meticulous examination of the donor's renal and genito-urinary system and a general medical evaluation. The last major requirement is that the donor have at least one kidney that has a single artery (demonstrated by arteriography) since double artery anastomosis is technically extremely difficult and the only situation in which Dr. Najarian will undertake such an operation is one in which the donor is an identical twin. We have also limited ourselves to ABO and Rh blood group compatible patients because a very high proportion of grafts are immediate failures when the blood compatibility barrier is crossed.

Having met these criteria—that is, a donor-recipient pair having been established—we must then proceed with preparation of the recipient. Since by intention we wait as long as we possibly can for the patient to have a useful life with conservative medical management, the patient is in a state of chronic advanced uremia by the time the decision is made and corrective measures must be carried out before the operation. In the course of long-standing, chronic uremia virtually every organ system is afflicted with profound disturbances, and it sometimes takes two and a half to three weeks to reverse these complex abnormalities. The azotemia itself must be controlled, since in some fashion most of the abnormalities of chronic uremia are a consequence of some poorly characterized nitrogen metabolites. Although chemically azotemia can frequently be controlled with a single dialysis, the effects on many of the organ systems are very slow to reverse and may take as long as two or two and a half weeks of optimal hemodialy-

sis control before we have satisfactorily reversed the abnormalities. The same holds for fluid and electrolyte abnormalities which with modern dialysis techniques can be quickly reversed; however, the more subtle changes—for example, long-standing abnormalities in intracellular pH and in intracellular ionic composition—probably are only gradually restored to normal.

Hematologic abnormalities consist not only of anemia but include a very significant bleeding tendency which exists in patients with chronic renal failure. Early in our experience, when operation was attempted after only a limited period of dialysis, the surgeons encountered excessive bleeding. Cardiovascular abnormalities consist of hypertension and our most feared complication, hemorrhagic pericarditis. This occurred in two of some 35 patients. In one of them open chest drainage was required, and in the other clotting of blood in the pericardial sac made thoracotomy necessary. Neuromuscular disorders are very prominent. Metabolic disorders consist of glucose intolerance and profound disturbances in protein metabolism which have gradually evolved over months or years.

DR. NAJARIAN: Our program of immunosuppressive therapy is more or less similar to that used in most other centers throughout the United States. At present we use one of the major antimetabolites—"Imuran,"[®] an imidazole derivative of 6-mercaptopurine.

I might just take a moment to talk about the action of these drugs, how and when we use them, and why we use them as we do. The antimetabolites as a general rule are basically analogues of various metabolites. Three are shown in Chart 3. Methotrexate is a folic acid inhibitor and the close chemical similarity between methotrexate and folic acid can be seen. The pyrimidine inhibitor 5-fluorouracil is similar to uracil, and 6-mercaptopurine is chemically similar to the purine, adenine. These antimetabolites act by competitive inhibition or by other routes which are poorly understood. However, the drug that we use most often is 6-mercaptopurine, actually in its imidazole form, "Imuran."[®] The way it acts is shown on a very simple chart of ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) synthesis (Chart 4). Beginning with simple precursors, the folic acid inhibition of methotrexate would block the incorporation of these carbon compounds into purine. The purine analogues or the antimetabolites that we are using,

| METABOLITE | ANTIMETABOLITE |
|---------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|
| <chem>OC(=O)CNC(=O)c1ccc(cc1)NCc2nc3c(nc(=O)n3c2N)O</chem> FOLIC ACID | <chem>OC(=O)CNC(=O)c1ccc(cc1)N(C)Cc2nc3c(nc(=O)n3c2N)N</chem> METHOTREXATE |
| <chem>Nc1ncnc2c1ncn2</chem> ADENINE | <chem>Nc1nc2c(ncn2C(S)N)c1</chem> 6-MERCAPTOPURINE |
| <chem>Oc1ccnc(=O)n1</chem> URACIL | <chem>Oc1cc(F)c(=O)n1</chem> 5-FLUOROURACIL |

Chart 3.—The natural antimetabolites and their parent compounds.

such as 6-MP, block the incorporation of the purine into polynucleotides either by substitution or by competitive inhibition, or they may affect the enzyme systems in a particular part of the chain of DNA synthesis. In like fashion the pyrimidine inhibitors act to block the pyrimidine that is being incorporated into the polynucleotides, such as DNA and RNA.

The following explains why these agents are so effective in transplantation and why the doses can be lowered to tolerable amounts in long-term patients. The clonal selection theory of antibody formation proposes that a lymphoid cell or a group of cells is committed to a specific antigen; further, that this group of cells continues to replicate with an intermitotic time of two to ten days or two to four days and that the group of cells remains fairly stationary in number. However, if an antigenic stimulus is given to this group of cells, there follows a rapid replication and exponential rise in the number of cells. Under these conditions intermitotic times can be shortened to four to six hours. By this means cells are formed in the vast numbers necessary to accomplish an immunological response against the foreign protein.

We suppress this cell replication in the following fashion: The day before transplantation we give Imuran,[®] the antimetabolite, then higher doses during the day of transplantation and for three or

four days after transplantation. By one week after operation the dose of the drug is down to tolerable levels for the patient, or about 3 mg per kilogram of body weight. We use as much as 6 to 7 mg per kilogram in the initial period when the graft is in place and the strongest antigenic stimulus is offered to the immunologically competent cells.

I have listed the three major agents in immunosuppression: (1) The alkylating agents that attack the DNA directly and in this fashion act very much like x-ray, (2) the antimetabolites, which block the synthesis of RNA and thereby block the ability of the lymphoid cells to divide, and (3) the actinomycin C and D and mitomycin apparently interfere with the transfer of information from nuclear DNA to nuclear RNA and block the formation, or

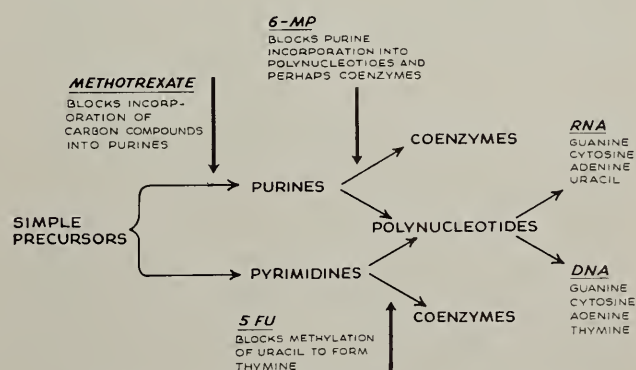


Chart 4.—Action of immunosuppressive drugs.

at least the production of messenger RNA from the nucleus. We give these agents at the time of rejection because we believe that at that time the cells are beginning to make antibody to attack the graft. In theory an ideal agent would be one such as puromycin, which actually attacks the protein synthetic mechanism; the proteins we are interested in are antibodies. Chloromycetin may act in the same way. If this is true, these may be very effective immunosuppressive agents when rejection occurs. Therefore, we use actinomycin at the time of rejection but give Imuran® from the very beginning.

In our program we also give corticosteroids before, during and after transplantation. This is not a common practice in other transplant groups. Two years ago we began to use corticosteroids early, in an effort to blunt an immunological response rather than wait for a rejection crisis to occur. In most persons receiving a kidney transplant, rejection will occur sometime within the first ten days to two weeks, despite immunosuppressive therapy with Imuran®. Corticosteroids are very effective in reversing the rejection process. With these agents, we thought we might even be able to abolish rejection crises altogether and permit some degree of graft-host adaptation to take place. We began using corticosteroids in high doses from the time of transplantation and reducing the doses sequentially thereafter. If rejection did occur, we gave corticosteroids in a slightly higher dose and then reduced the amounts once again. We are still not quite sure how they act. Their action may be related to their lympholytic or their anti-inflammatory properties; or they may act because of their membrane-stabilizing qualities. We have studied this problem in our laboratory. We did kidney transplants in eight dogs and, using *in vivo* and *in vitro* techniques, we found that there is a significant amount of antigen in the renal vein effluent. At four hours after transplant, six of the eight dogs had free antigen in the plasma issuing from the kidney. At two days, four had antigen in this fluid. We used this observation to study the effect of corticosteroids and found that they did indeed reduce but did not eliminate the amounts of antigen excreted.

In other studies we found that when the injury to the kidney was increased, either by prolonging ischemia or by exposure to x-ray, the amount of antigen that issued from the kidney increased. We then gave corticosteroids to a group of dogs. In these preliminary studies, three animals were given

prednisolone (50 mg a day) before and after transplantation. In one animal we found antigen after four hours and at one day, in the second animal at two days and none at all in the third, certainly not after the two-day period. The amount of antigen that issued from these kidneys seemed to decrease in the dogs treated with corticosteroids. These studies are going to be confirmed by *in vitro* analysis of the antigen, which we hope will be a more accurate technique.

As a result of these observations we believe that the corticosteroids do have an effect on stabilizing membranes, thereby decreasing the amount of antigen from the kidneys. Perhaps for this reason we are able to abrogate at least partially the immune response that has occurred with rejection as early as ten and fourteen days. With corticosteroids our average time of early rejection, when it does occur, is 37 days, and it is very mild and easy to control. We think that this is a real addition to the immunosuppressive therapy regimen.

Immunosuppressive drugs are not ideal agents. Drug toxicity and sepsis are still major causes of death. What looks best in the future, if we again look into our crystal ball, is the antilymphocytic serum now used by several investigators, including the group at the Massachusetts General Hospital, and Dr. Woodruff in Edinburgh. Although antilymphocytic serum will reduce the total lymphocyte count to the same degree as thoracic duct drainage or intravascular radiation, it is a more effective immunosuppressive agent. Some investigators, such as Sir Peter Medawar, feel that perhaps the antiserum masks the immunologically competent cells so that they do not recognize the tissue as a foreign invader and do not attack it. This may be rather fanciful but, from animal experiments, it appears that this is what is going on. Many provocative experiments tend to support this. When antilymphocytic serum will become available for clinical use is dependent upon many factors; and the use of heterologous serum in humans presents its own problem—that of immunologic reaction. It looks as if there may be a ray of hope in this type of immunosuppression, which is different from chemical immunosuppression and is a direct immunological type of immunosuppressive attack.

The other problem with immunosuppressive drugs occurs in identical twins. There should be a 100 per cent success rate with homotransplantation in identical twins, for there is no immuno-

logical barrier; but the success rate across the country is still only about 66 per cent. Because of these disappointing results we have examined the kidneys in our cases of this kind and have re-read the original reports of Murray and his associates which indicated that in one or two of the cases of transplants from identical twins, glomerulonephritis had developed in the newly transplanted kidney when the recipient identical twin had glomerulonephritis. If the recipient had pyelonephritis or polycystic kidneys, glomerulonephritis did not develop. Apparently in almost 80 per cent of these recipient identical twins with glomerulonephritis, glomerulonephritis developed later in the transplanted kidney. In homotransplants between non-identical twins in which immunosuppressive therapy was given, only two questionable cases of glomerulonephritis have been seen. Our experience now extends for some three years, so we are well within the time when we should see glomerulonephritis if it is going to develop. The only difference between these two groups is that one is given immunosuppressive therapy and the other is not. We have recently been taking fluorescent photomicrographs of the kidneys that are removed. We have found, as have other investigators, that there is an immunological component to glomerulonephritis. We can routinely show fluorescence, either with antiserum to complement, to 7-S γ globulin or even to M γ globulin that localizes in the basement membranes of the glomeruli of all kidneys involved with glomerulonephritis. A similar thing can be found with the patients with lupus erythematosus but not in those with pyelonephritis. An identical twin is scheduled for transplantation in our program and we will probably give this patient modest doses of immunosuppressive drugs in the postoperative period.

DR. PAUL GULYASSY: Dr. Najarian is so atypical a surgeon that he has not even bothered to tell you the details of how the operation is performed, but we will assume that everything has gone very smoothly and successfully and that the patient is now in the postoperative state. About 14 months ago when we last reviewed our results at Medical Rounds, we had reached a total of 14 patients in our series. In looking at our results as well as the world results, there was one fact that was very striking. That is that early failures—grafts that either failed to function at all or that functioned initially but failed within the first 48 hours—still make up a very important proportion of graft fail-

ures. As we studied this problem over and over we could find no reasonable explanation for these early failures. One usual explanation for early failures, renal ischemia, hardly seemed applicable to our experience. The average ischemia time of 21 minutes achieved for this group of patients by Dr. Najarian was well under what is considered the safe limit. In addition, we have not used blood incompatible donor-recipient pairs and the usual type of explanation that perhaps these early failures represented pre-sensitization of the recipient did not seem to have any valid basis in either experimental fact or in any actual measurements in patients.

As we further considered the possible causes of these early failures and how we might prevent such failures, one fact emerged which was very striking. That is that although there are several hundred living patients who have had renal transplants, there is not a single report of what happens to the donor kidney during the course of nephrectomy. We thought that it would be wise to take a look at the function of the donor kidney as the surgeon is isolating it and preparing it for removal. We therefore undertook to observe patients during nephrectomy and it soon became very apparent that we must pay very close attention to what is going on with the donor kidney during nephrectomy. For example, we observed in the first patient we studied that shortly after anesthesia, as is well known, striking oliguria occurred as a consequence of the fall in blood pressure which occurs with induction. In addition to this functional effect we found evidence of renal injury occurring despite very careful attempts by the surgeon to be as atraumatic as possible when handling the kidney and its arteries. We found up to 2 plus proteinuria occurring as soon as the surgeon handled the renal pedicle; in addition, there was striking hematuria and cylindruria. In this patient a more alarming fact was that for approximately 30 minutes preceding actual nephrectomy no urine appeared in the bladder.

After these observations we have introduced two major changes in our program. First, urine output is continuously followed throughout the nephrectomy and the surgeon is notified if it falls below 1.0 ml a minute. Second, we instituted a program which was somewhat of a shotgun approach, of necessity, in which we incorporated all possible measures that we felt might protect the donor kidney from intraoperative injury, which

then is followed by a period of unavoidable injury during approximately 20 to 25 minutes of total deprivation of blood as perfusion, cooling and anastomosis of the kidney is performed. What we did was to hydrate the patient, or I should say that we corrected the normal surgical dehydration associated with enemas and thirsting over night, by infusing the patient with 15 ml of half-normal saline solution per kilogram of body weight during one hour before anesthesia. Second, the anesthetist carefully maintained normal blood pressure by continuous fluid replacement and plasma replacement where necessary. Third, when despite these measures urine output fell early in the course of operation, we injected modest amounts of mannitol (12.5 gm) to induce a mild osmotic diuresis. Then, just before clamping of the kidneys, we injected a second dose of mannitol to reduce the concentration of coagulable materials as well as potential toxins to a minimum and perhaps also to prevent the very rapid collapse of the tubular lumen which is known to occur after cessation of filtration. The results of these measures have been truly striking. In our early experience, we as others had a failure rate of about 40 per cent within the first 48 hours. Among the last 20 patients (with the exception of one who had a problem with a tortuous vein), we had no initial failures. We have no observations on the patients operated on before the institution of these measures, but some observations that Dr. Duffy collected from the two kidneys simultaneously and separately in a recent group show the magnitude of the depression of renal function which still persists despite these measures. Table 2 compares the urine output in five donors from the ureter of the kidney which is about to be removed and from the contralateral side as measured by the bladder output. With one exception there is a striking difference just before nephrectomy in the urine output from the two sides; for example, 15 ml per minute against 4 ml per minute, 3 against 0.5, 6 against 1.3, and 2.5 against 0.3.

TABLE 2.—*Urinary Output Immediately Before Nephrectomy*

| <i>Consanguineous Donor No. (CD)</i> | <i>Donor Kidney (ml/min)</i> | <i>Remaining Kidney (ml/min)</i> | <i>Ratio: $\frac{R^*}{D}$</i> |
|--------------------------------------|------------------------------|----------------------------------|------------------------------------------|
| 18 | 4.0 | 15.0 | 3.75 |
| 19 | 0.5 | 3.0 | 6.00 |
| 22 | 1.3 | 1.1 | 0.84 |
| 23 | 1.3 | 6.0 | 4.8 |
| 24 | 0.3 | 2.5 | 8.3 |

Mean 4.7

*R=Remaining kidney; D=Donor kidney (to be transplanted).

The effects of this change in attention to the donor during nephrectomy in terms of renal function early and subsequently is shown in Table 3 in which the mean creatinine clearances for our initial group, who received routine preoperative and intraoperative management, were compared with clearances in a subsequent group who were managed with measures to protect the kidney from injury. The mean clearance at 12 hours rose from approximately 20 ml in the initial group to 60 ml in the donor-treated group. There still was a striking difference at three days and seven days. Beyond seven days, where we included only the survivors from the initial group—the surviving 60 per cent—the difference began to disappear. Therefore the survivors did go through a course of tubular necrosis of a reversible nature but ultimately had reasonable function.

The effects of this virtual elimination of initial failures is shown in an increase in over-all survival in the second group over the first. Where at the end of seven days in our first series we were dealing with a survival rate of approximately 70 per cent, and of about 55 per cent at 40 days, we are at 100 per cent in the second group. There persists an attrition beyond 40 days which is now clearly an immunological rather than a renal and hemodynamic problem, and it remains the major problem for solution in clinical transplantation.

DR. NAJARIAN: The classic signs of rejection include fever, leukocytosis, pain or tenderness over

TABLE 3.—*Comparison of Mean Creatinine Clearance Values in Group A and Group B**

| | <i>Creatinine Clearance</i> | | | | | |
|----------------|-----------------------------|---------------|---------------|----------------|-----------------|---------------|
| | <i>12 Hours</i> | <i>3 Days</i> | <i>7 Days</i> | <i>40 Days</i> | <i>6 Months</i> | <i>1 Year</i> |
| Group A | 23.2 (7.6)† | 28.7 (8.9) | 33.5 (9.5) | 52.8 (12.7) | 67.2 (13.6) | 56.8 (12.1) |
| Group B | 61.2 (6.0) | 59.6 (5.1) | 61.8 (3.9) | 67 (6.1) | 67.7 (6.1) | 81.33 (6.8) |
| p values | <0.01 | <0.01 | <0.01 | <0.4 | >0.9 | <0.2 |

*Group A=The initial group who received routine preoperative and intraoperative management. Group B=Subsequent group who were specially treated to protect the kidney from injury.

†Standard Error.

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the kidney and perhaps myalgia and arthralgia. If we blunt these signs with corticosteroids, we must look for much more subtle signs of rejection. The earlier that rejection is diagnosed, the more effectively can it be treated. Therefore, we have examined two indications of kidney damage which may occur earlier than gross alteration of renal function; these are a rise in serum creatinine and a fall in creatinine clearance. We have recently reported on work that has been done with Dr. Noble. We have found, both experimentally and clinically, that lysozymes in the urine are a very good indication of tubular damage. We have been measuring urinary lysozymes in all of our patients. For a while we measured serum lysozymes but found them to be quite erratic. The urinary lysozymes may represent the tubular lysozyme content that goes down into the urine, so that this is a potentially direct measurement of tubular damage. In addition, it has long been known that proteinuria, protein in the ultrafiltrate from the kidney, is a sign of glomerular damage. The Masugi nephritis experiments showed this very nicely in the case of a purely glomerular lesion. The first signs of this are

evident from the protein in the urine of the rats so treated. So we have two measurements we can use to detect some degree of destruction in the kidney: Lysozymuria and proteinuria.

Chart 5 gives pertinent data on a girl who is now approximately 20 months post-transplantation of a kidney from her mother. We have plotted on the ordinate the urinary lysozymes in mg per ml, urine proteins in grams per 24 hours, creatinine clearance, serum creatinine, urine outputs and prednisone dosage. On the day of transplantation and shortly thereafter, in all of our patients, there is a very high lysozyme content in the urine, which is indicative of the degree of tubular damage that occurs from the relative ischemia in the donor and the absolute ischemia imposed during transplantation.

In this particular patient, who is in the first group that Dr. Gulyassy discussed, there was severe tubular damage. The lysozyme did not return to normal for some ten days. In addition, there was a very slow rising creatinine clearance indicative of a damaged kidney that was slowly recovering. When the first rejection crisis occurred, there

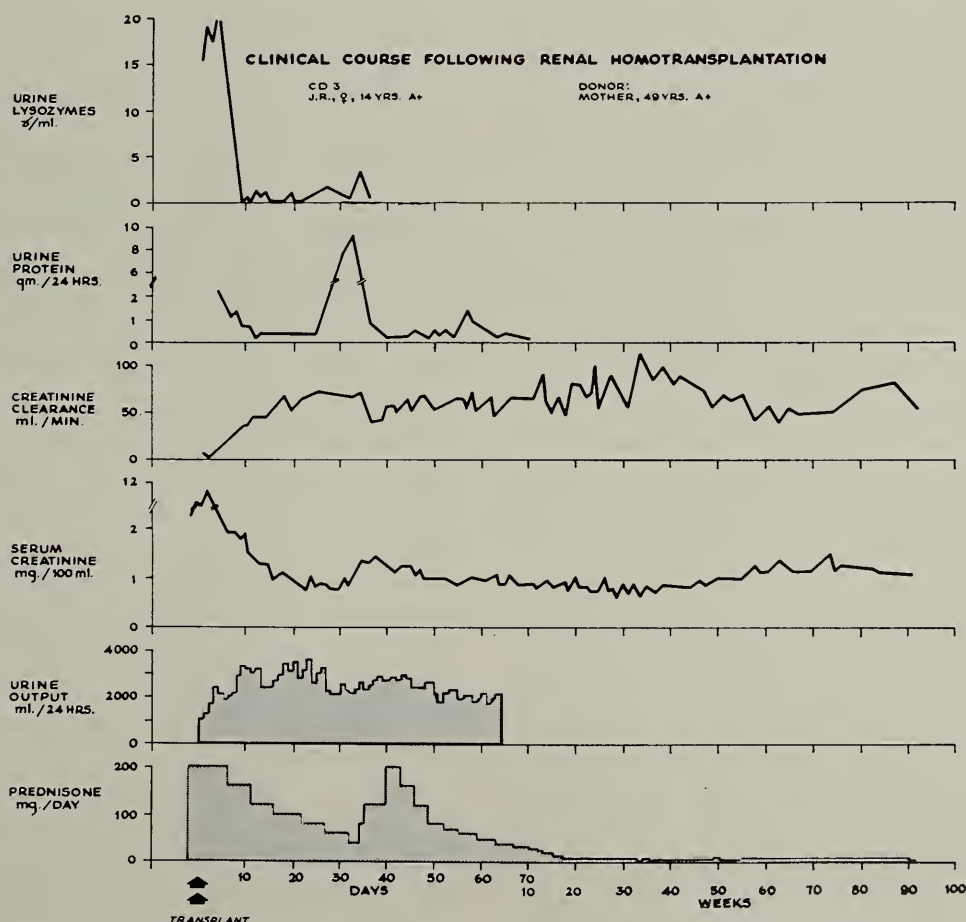


Chart 5.—Clinical course following renal homotransplantation in a girl 14 years of age. Donor was her mother, 49 years of age.

was a very subtle change in the serum creatinine and a definite drop in the creatinine clearance. This was preceded by a significant rise in urinary protein, to 6 or 7 grams in 24 hours.

In this patient the pattern of rejection was mainly that of proteinuria and, we would judge, primarily a glomerular type of lesion. Eventually the rejection process became manifested by a rise in the creatinine and fall in the clearance. This was treated by increasing steroids, actinomycin C and local radiation to the kidney. The patient survived this particular rejection crisis and is doing perfectly well, with satisfactory clearance and a good serum creatinine. She is now taking 7.5 mg of prednisone a day.

Let us take another example, a case in which there was a prompt fall in serum creatinine, and lysozymes fell to normal levels by about the eighth day. A slowly rising creatinine clearance indicated some degree of damage to the kidney. Everything went along fairly well; the serum clearance was 1.5 to 2 mg per 100 ml, and the creatinine clearance was fairly good. By the seventieth or eightieth day, there was a definite rejection reaction. There was a decrease in the urinary output followed by a rise in the serum creatinine and a fall in the creatinine clearance. This occurred several days after the lysozyme level rose. This is predominantly a tubular type of rejection pattern, marked by a very high urinary lysozyme level and modest degree of proteinuria, predominantly glomerular in origin. The other was manifested by lysozymuria, or a tubular lesion. When we measure lysozymes and protein in the urine, we find these reflect rejection approximately a day before we see the changes in creatinine clearance. At the earliest signs of this damage treatment is begun.

Many of the "rejection crises" that we have seen or treated were in fact not rejection crises. We were misled by infection on several occasions. We have been fooled by other things. We are fooled less frequently now. One finding that we reported recently is fat embolization that occurs following use of corticosteroids. There is also a possibility of fat embolization to the kidney with decreased function, which simulates a rejection crisis. We have had several such cases. Two patients actually had embolization to the kidney. One was reported in the *New England Journal of Medicine*. This patient's kidney was functioning well for approximately four months, then there was a rapid fall in the creatinine clearance and a rise in serum crea-

tinine. When arteriograms were obtained, a very peculiar pattern was seen. The arterioles going out into the kidney formed little puffs and in areas throughout the kidney there was no contrast medium. The only thing that can cause this is embolization. A biopsy of the kidney showed that it was perfectly normal in these areas, but in the intermediate areas there was massive necrosis. In true rejection, we must find the earliest signs of rejection and treat them as promptly as possible with steroids, actinomycin and local radiation. Crises that occur late are easy to reverse, for the most part.

We would now like to present three cases. In the first the patient is a boy who is approximately two years post-transplantation and is now going to school. The second case was presented to you last year; the patient is now approximately 20 months post-operative. The third patient is a young woman who received a transplant just 14 days ago. Dr. Gilbert Ashor, who is on the Transplant Service, will present the patients.

DR. GILBERT L. ASHOR^{*4}: The first patient we would like to present today [introducing him] is a young high school student who was 16 years old at the time of renal transplantation, and is now 17. At age 12 he was discovered to have proteinuria. He did well, however, and was asymptomatic until age 15, four months before his admission to University of California Hospital. At that time he had blood nitrogen of 230 mg per 100 ml and a serum creatinine of 15.6 mg per 100 ml. Peritoneal dialysis was performed several times before bilateral nephrectomy-splenectomy was performed 7 April 1964. Two weeks later his mother's left kidney was transplanted in him. The total "ischemic time" during the operation was 25 minutes and the patient's postoperative course was complicated by a mild rejection crises in August and again in December 1964. He received actinomycin, radiation therapy to the transplanted kidney and large doses of prednisone. Currently, the patient is receiving 100 mg of 6-mercaptopurine (Imuran®) and 7.5 mg of prednisone daily.

DR. NAJARIAN: The patient is now a senior in high school and is fairly active in school and extracurricular activities. Bobby, what do you participate in at school?

^{*4}Resident in Surgery.

PATIENT: I participate in the sports we have in physical education and extra activities after school.

DR. NAJARIAN: He also wrestles and weight-lifts. We place no real physical restrictions on these patients. While the patient is here, are there any questions that anybody in the audience would like to direct to him?

DR. WILLIAM A. ATCHLEY*⁵: Do you instruct him about severe dehydration?

DR. NAJARIAN: No, we have not.

DR. ATCHLEY: Do you think you should?

DR. NAJARIAN: We believe that these kidneys can concentrate and dilute as well as any other kidney. We see no reason why special precautions should be taken.

DR. SMITH: Has he had any problem with infections over the last two months?

DR. NAJARIAN: Have you had any infections?

PATIENT: I don't think so.

DR. NAJARIAN: He has had none. These patients have been exposed to measles, chicken pox, all the viral and bacterial infections, and they have resisted these very well.

DR. ASHOR: The next patient to be presented is a housewife, 49 years of age, who was well until her first symptom developed in June of 1963. At that time she had weakness, nausea, vomiting and fatigue, and she entered the hospital. A diagnosis of severe anemia was made and multiple blood transfusions were given. In February of the following year, 1964, the same symptoms developed again and a diagnosis of uremia was made. The serum creatinine level was 17.2 mg per 100 ml. She was subsequently admitted to the University of California Medical Center, where a renal biopsy showed medullary cystic disease. She had multiple hemodialyses, and on 7 July 1964 she underwent a combined procedure including bilateral nephrectomy-splenectomy, and received a transplanted kidney from a donor brother. The total time of ischemia was 24 minutes. On the first day postoperatively the serum creatinine was 2.4 mg per 100 ml and the second day postoperatively it was 0.9. The patient is currently receiving 75 mg of Imuran® and 7.5 mg of prednisone daily.

*⁵Associate Professor of Medicine.

DR. NAJARIAN: This is one of our more remarkable patients. We once thought that we should not perform transplantation on people over the age of 45, but as a result of this patient's success, we are reconsidering this notion. The remarkable thing was her determination to get well. On the first postoperative day after a procedure that lasted six or seven hours, Dr. Gulyassy and I walked into her room and she was reading the newspaper and eating breakfast. We thought that she might have some trouble later, but she continued to do well. She has never had a rejection crisis and it is now almost two years since the operation. She now travels around the Central Valley area to give talks on transplantation to various groups, and she borrows our slides from time to time. We try to keep her up to date on current developments in transplantation. (Addresses patient): How do you feel?

PATIENT: Wonderful.

DR. NAJARIAN: This is a complete summary. Would anyone like to ask her questions? She works about 14 hours a day, running a bicycle shop in Madera. Have you had any problems from your kidney transplant?

PATIENT: None.

DR. NAJARIAN: In answer to Dr. Smith's question about infection, several suture abscesses with staphylococcal infections did develop. The abscesses were easily controlled, incised and the sutures were removed without any difficulty.

DR. ASHOR: Our last patient is the most recent to have a transplant. She is a 21-year-old coed from UCLA. The patient was well until, in the summer of 1961 contact dermatitis developed and was followed by leg edema which progressed to anasarca. In August of 1961 she was discovered to have albuminuria, hematuria and casts in the urine. A diagnosis of nephrosis was made. She was treated with prednisone and chlorothiazide and remained well for the subsequent four years except for periodic ankle edema and easy fatigability. In November 1965 she was again seen for severe epistaxis and at that time was discovered to have a packed cell volume of 23 per cent, blood urea nitrogen of 125 mg per 100 ml and serum creatinine of 11.3 mg per 100 ml. In December of 1965 she entered the hospital with similar findings: Anemia, blood urea nitrogen of 216 mg per 100 ml and serum creatinine of 16.4 mg per 100 ml. An intra-

venous pyelogram showed bilateral contraction of the kidneys, and a diagnosis of chronic glomerulonephritis was made. Multiple hemodialysis was carried out. On 23 February 1966 bilateral nephrectomy and splenectomy were done and on 2 March 1967 a kidney from her mother was transplanted in her. Her postoperative course has been one of very steady and gradual improvement, uncomplicated by any reaction. Serum creatinine on the morning of operation, after hemodialysis, was 12.4 mg per 100 ml. On the afternoon of operation it was 5.6 mg and on the day following it was 2.6 mg. Subsequently the serum creatinine ranged between 1 and 1.4. Creatinine clearance has steadily risen from a low of 26 to 60 ml per minute. The patient is receiving Imuran,[®] 150 mg, prednisone, 50 mg, and Aldomet,[®] 2 gm daily.

DR. NAJARIAN: The patient is now two weeks postoperative. (Addresses patient): How have you been since the operation?

PATIENT: Really good. I feel wonderful.

DR. NAJARIAN: The girl is a bacteriology student in her senior year at UCLA, so perhaps some day we can get some help from her from the bacteriological point of view. Are there any questions anybody would ask the patient?

DR. SMITH: What are the major changes that she has noticed since the operation?

PATIENT: The first week I was kind of sore, but I have had a lot more energy than I have had in a long, long time. I think it started about the first day after operation; I could feel it—a gradual increase in energy.

DR. NAJARIAN: Thank you for coming to see us. We wanted to show these three patients in three different lights: One, the young boy who about

255 days after transplantation had a rejection crisis which was mild and easy to reverse. He has had no subsequent difficulties. The second patient had a sibling donor and there was no rejection crisis at all. And finally, a patient just recently operated upon.

DR. SMITH: I think we would all agree that these are splendid results and that this was a superb presentation. I would like to say personally that if Dr. John Najarian ever undergoes any rejection crisis in Surgery we would be very delighted to welcome him into Medicine. Perhaps we have time for one or two comments or questions.

UNKNOWN PHYSICIAN IN AUDIENCE: What is the present status of second transplants?

DR. NAJARIAN: Second transplants are about the same as first transplants. For awhile they looked like they were even better. Of course you would suspect that they may go a little quicker because of pre-sensitization, etc. It turns out that some degree of tolerance is obtained with the first transplant. We thought it would be better, but now, with more of them being done, they appear to be about the same.

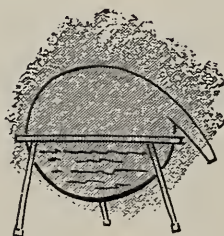
DR. MAURICE SOKOLOW*⁶: Does the behavior of the blood pressure help you predict the likelihood of rejection?

DR. NAJARIAN: This is a very interesting question. We don't know if the blood pressure rises because of our treatment with steroids or because of the disease. We think it is because of the disease. Almost uniformly, when rejection occurs, there is an increased need for anti-hypertensive medications.

GENERIC AND TRADE NAMES OF DRUGS

6-mercaptopurine—*Imuran*.[®]
Methyldopa—*Aldomet*.[®]

*⁶Professor of Medicine.



Varicella Pneumonia

A Report of 20 Cases, with Postmortem Examination in Six

E. NICHOLAS SARGENT, M.D., *Los Angeles*, MERL J. CARSON, M.D., *Orange*,
AND EMMETT D. REILLY, M.D., *Los Angeles*

■ *Twenty cases of primary varicella pneumonia, 16 in adults and four in children, were studied. Two adults and four children died, two of the latter with complicating bacterial infections. In two patients the primary cause of death was severe alveolar-capillary block. Staphylococcal septicemia, midbrain hemorrhage and meningoencephalitis were primarily responsible for death in other patients.*

Radiologically, the lungs showed diffuse, poorly marginated, nodular lesions, often peribronchial in location, more easily defined in the thinner peripheral lung fields, with an alveolar acinar pattern, tending to coalesce in the hilar and perihilar regions. Pathologically, the cutaneous varicella lesions were matched by similar lesions regularly found in the lungs and pleura, as well as the peritoneum and the liver. The pulmonary nodular lesions corresponded to alveoli, filled with precipitated protein and active inflammatory cellular material, surrounding the bronchioles, which themselves were often involved, and these in turn were surrounded by areas of normally aerated alveoli.

Eleven moderately to severely ill patients were treated with antibiotics, six moderately to extremely ill were treated with antibiotics and adrenal cortical steroids. There was no evidence of significant change in the course of the disease resulting from use of steroid therapy.

AS CHICKENPOX IS usually a benign, contagious disease, it is not generally appreciated that, especially in adults, severe varicella pneumonia and associated complications may prove fatal. The first American report of autopsy findings in systemic varicella was written by Johnson¹⁸ in 1940, who observed focal necrosis in the skin, esophagus, pancreas, liver, renal pelvis, ureters, bladder and adrenal glands of a 7-month-old infant who died of the disease. Detailed case re-

ports and reports of small series have subsequently documented findings in fatal cases.*

Although Krugman²⁰ emphasizes that varicella pneumonia (associated with virus infection) is rarely encountered in the pediatric age group, pulmonary involvement has been described in newborn infants,^{2,22} in cases of congenital chickenpox²⁴ and in children who have contracted chickenpox while receiving steroid therapy for another disease. In general, however, pulmonary complications in childhood usually are in con-

Submitted 17 February 1967.

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*Reference Nos. 6, 8, 12, 20, 22, 24, 25.

TABLE 1.—Clinical and Laboratory Findings in 20 Cases of Primary Varicella Pneumonia

| Case | Age Years | Sex | Cough | Respira- tory Rate | Cyanosis | Hemoptysis | Rales | Breath Sounds | Chest X-ray Ab- normalities | Treatment | | | Complications |
|------|--------------|-----|-------|-----------------------|----------|------------|-------|------------------|-----------------------------------|------------------------|------------------|---------|--------------------------------------------------------------------------------------------|
| | | | | | | | | | | White Cell Count | Anti- biotics | Steroid | |
| 1 | 54 | M | ++ | 70 | ++ | 0 | ++ | D | No x-ray | 13,600 | + | 0 | Died after 9 hr. Midbrain hemorrhage. Cardiac arrest. |
| 2 | 35 | F | ++ | 60 | ++ | + | ++ | D | ++ | 12,500 | + | + | Died after 14 hr. Varicella pneumonia and hepatitis. |
| 3 | 4 | M | ++ | 80 | ++ | 0 | ++ | D | ++ | 9,600 | + | 0 | Died after 8 hr. Osteomyelitis, Staphylococcal Sepsis. |
| 4 | 6 | M | ++ | 90 | ++ | 0 | 0 | N | ++ | 6,900 | + | + | Died after 3 days. Hypogammaglobulinemia, Staphylococcal Sepsis, Encephalitis. |
| 5 | 2½ | F | ++ | 42 | ++ | 0 | ++ | D | ++ | 20,100 | + | 0 | Died after 26 hr. Varicella pneumonia, hepatitis and cerebral edema. |
| 6 | 3 | M | + | 44 | + | 0 | 0 | N | No x-ray | 19,100 | + | 0 | Died after 4 hr. Viral encephalitis, Cerebral edema, Necrosis spleen and liver, pneumonia. |
| 7 | 37 | F | ++ | 72 | ++ | + | ++ | D | ++ | 19,400 | + | + | None. |
| 8 | 28 | F | ++ | 50 | ++ | 0 | ++ | D | ++ | 9,800 | + | 0 | None. |
| 9 | 26 | M | ++ | 52 | ++ | + | ++ | N | ++ | 16,300 | + | 0 | Thrombophlebitis. |
| 10 | 41 | M | ++ | 44 | + | + | ++ | D | ++ | 7,400 | + | 0 | None. |
| 11 | 30 | F | + | 30 | + | + | 0 | D | ++ | 6,100 | 0 | 0 | None. |
| 12 | 43 | F | ++ | 32 | 0 | 0 | ++ | D | ++ | 8,100 | + | + | None. |
| 13 | 28 | M | ++ | 32 | 0 | + | ++ | D | ++ | 8,800 | + | 0 | None. |
| 14 | 27 | M | ++ | 35 | 0 | 0 | + | N | ++ | 8,300 | + | 0 | None. |
| 15 | 37 | M | ++ | 35 | 0 | + | 0 | D | ++ | 6,500 | + | 0 | None. |
| 16 | 24 | F | ++ | 55 | 0 | 0 | 0 | N | ++ | 6,800 | + | + | None. |
| 17 | 38 | M | ++ | 45 | 0 | 0 | 0 | N | ++ | 5,950 | + | 0 | None. |
| 18 | 32 | M | ++ | 34 | 0 | 0 | 0 | D | ++ | 15,400 | + | + | None. |
| 19 | 33 | F | + | 30 | 0 | 0 | 0 | N | ++ | 6,500 | 0 | 0 | None. |
| 20 | 40 | M | ++ | 20 | 0 | 0 | 0 | D | ++ | 7,300 | 0 | 0 | None. |

+++ = Severe; ++ = Moderate; + = Mild; 0 = Absent; N = Normal; D = Decreased;

nection with a bacterial disease, and hemolytic staphylococcus aureus is the most frequent offender.²⁰

Estimates of the incidence of varicella pneumonia range between one and eight per thousand cases of chickenpox.^{5,9,10} It is generally agreed that adults, although approximately ten times less susceptible than children, are more prone to this complication,⁷ the incidence running as high as 16.5 per cent of total adult cases.^{31,32}

Our clinical experience and findings in patients with primary varicella pneumonia, and associated complications, will be described.

Material

During the past six years, 20 patients (Table 1) with the diagnosis of varicella pneumonia have been treated at our hospital. They were all admitted to hospital and were carefully observed and treated by house physicians and senior staff members.

Symptoms

The onset of symptoms occurred three to seven days before hospital admission. Fever was always the first manifestation and was present in all cases, ranging from 38.8° to 41°C (102° to 106°F). Adults commonly complained of "chills" and aching in muscles and back. A typical varicella skin rash appeared on the second or third day and was very severe in every case. Cough was always present and hemoptysis and inspiratory chest pain were present in seven (35 per cent). Dyspnea was present in 16 cases (80 per cent) one to two days before admission.

Physical Findings

Physical examination on admission revealed dyspnea in all but one case, respirations varying from 20 to 90 per minute. A severe varicella skin rash that also involved mucosa of the mouth and pharynx was present in all cases. Body temperature was elevated in all but one patient. The maximum at the time of admission was 40.6°C (105.2°F). Cyanosis of skin and buccal mucosa was obvious in 11 patients (55 per cent). One patient was disoriented and one was comatose. Pulmonary rales were present in 11 cases (55 per cent) with decreased breath sounds in 12. Five patients had no auscultatory evidence of pulmonary disease, and yet roentgenographic study in each case revealed findings of severe, bilateral pulmonary infiltration.

Laboratory Findings

Routine laboratory investigations revealed leukocytes numbering 5,950 to 20,100 per cu mm with the count less than 10,000 in 13 cases. Differential leukocyte counts were within normal limits in half of the cases, with a slight to moderate left shift in the remainder. Blood cultures were positive in two children (hemolytic staphylococcus aureus), one with associated osteomyelitis and the other hypogammaglobulinemia with sepsis.

X-ray Examination

Two patients (cases 1 and 6) died before chest x-rays could be obtained. Four of the 20 patients had moderate radiographic changes associated with moderate clinical findings. The remaining 14 had severe and extensive radiographic findings.

Although the roentgenographic findings differed in some detail, they were similar enough to define a fairly characteristic pattern. Diffuse miliary or nodular patterns were seen throughout both lung fields. Although the nodules generally were approximately 0.5 cm in diameter, there were variations from that size. The nodules were superimposed upon considerably increased bronchovascular markings and they appeared separate and distinct from surrounding tissue, especially in the thinner, peripheral lung fields. Nodular coalescence occurred particularly in the hilar and perihilar regions. The nodular alveolar infiltrates were actually acinar nodular lesions with fluffy, indistinct margins (Figure 1).

Transitory changes were common and the appearance changed rapidly in several cases. Some

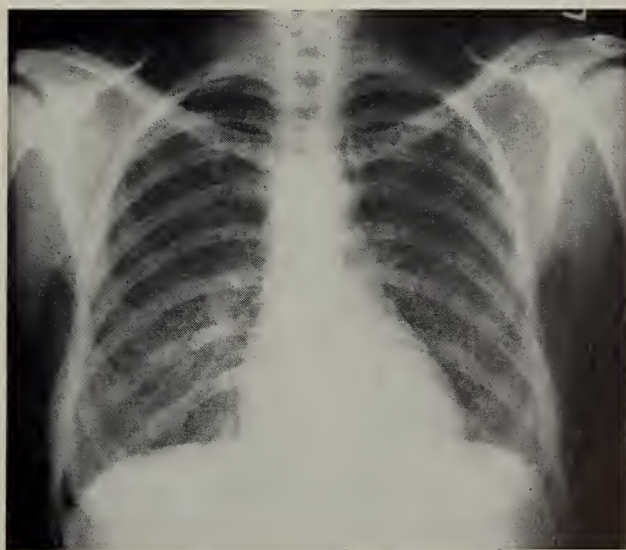


Figure 1.—X-ray film of chest showing varicella pneumonia in patient with widespread cutaneous lesions.

areas of nodulation resolved as other new areas appeared. Coalescence of nodules produced patchy areas of consolidation, especially at the lung bases. No portion of the lungs was spared, although the densities appeared heavier in the perihilar regions and gradually diminished toward the periphery. In addition, the lung roots and hilar shadows were increased in prominence and some were increased in size. Nodular hilar adenopathy in two cases subsided as the pulmonary nodulation resolved. Generalized lymphadenopathy was also noted in these two cases. One case showed blunting of the costophrenic angles associated with a small amount of pleural fluid, which cleared rapidly within a few days.

Hospital Course

The patients may be divided into three clinical categories.

1. Three patients were only moderately ill, with radiographic findings of pneumonia, but no initial auscultatory pulmonary abnormality. Very minimal cyanosis was found in one patient, who required supportive therapy with oxygen. They were otherwise treated symptomatically. Two patients improved rapidly and appeared clinically well by the third hospital day. In one, pulmonary rales and hemoptysis developed on the day following admission. She too, appeared clinically well on the third day although pulmonary rales persisted until the sixth hospital day.

2. Eleven patients were moderately to critically ill on admission and were treated with oxygen and antibiotics (penicillin and streptomycin, tetracycline, achromycin or chloramphenicol). Seven survived and four died. Admission temperature of the survivors ranged from 38.6°C to 40.5°C (101.6°F to 105°F) and returned to normal in two to five days (average three days). Respirations ranged from 30 to 52 per minute. Cyanosis was present in one adult with arterial oxygen saturation of 77 per cent and vital capacity of 700 cc. The cyanosis disappeared in three days, vital capacity rising to 1,400 cc on the fourth day and to 2,250 cc on the ninth day. Sputum and throat cultures revealed no pathogens. Abnormal pulmonary roentgenograms were present in each case although in two patients the lungs were normal to auscultation at the time of admission. In one of these patients pulmonary rales and hemoptysis developed on the second day of therapy. Pulmonary rales disappeared by

the sixth day in all but one patient (in whom they persisted for 12 days). The only complication was thrombophlebitis, in one patient, resulting from intravenous catheterization for parental fluid administration.

In this second group, four patients died within 26 hours after admission. At admission each was critically ill with cyanosis and dyspnea. In one, pneumonia and resulting alveolar-capillary block clinically appeared to be the cause of death. In the remaining three, additional organ involvement seemed most important in contributing to the immediate cause of death. Pronounced cerebral edema without encephalitis was present in one case; petechial midbrain hemorrhage and cardiac arrest in one; staphylococcal sepsis and osteomyelitis was present in one patient, a 4-year-old boy; and one patient had pronounced meningoencephalitis with respiratory depression.

3. Six patients on admission were moderately to extremely ill and received oxygen, antibiotics and adrenal steroids (hydrocortisone or prednisone or both). Four survived and two died. Admission temperature of the survivors ranged from 38.6° to 39.9°C (101.4° to 103.8°F) and returned to normal in from one to four days (average two and three-quarters days). In two patients, the temperature precipitously dropped to normal, in one case eight and in the other 20 hours after admission. Respirations ranged from 32 to 72 per minute and also returned to normal within four days. Clinical cyanosis, arterial oxygen desaturation (83 per cent) and decidedly reduced vital capacity (330 cc) was noted in two adults. Administration of steroids was begun on admission but cyanosis persisted for three days and four days. Pulmonary rales were present in three patients and persisted for two, six and seven days. They were never present in the fourth patient, in spite of dyspnea and radiographic evidence of pulmonary disease.

Of the two patients who died in this third group, one was a 6-year-old boy who had been under therapy for Burton's type hypogammaglobulinemia and had previously had repeated, severe bacterial infections. He died after three days with varicella pneumonia, hepatitis, meningoencephalitis and hemolytic staphylococcus septicemia. The second patient was a 35-year-old woman who died 14 hours after admission, of varicella pneumonia and hepatitis.

Postmortem Examinations

Six cases were fatal and postmortem examinations were performed. Severe skin involvement was present in all of them. Visceral lesions resembled those of the skin, modified by the tissue response in various areas. Varied lesions found in a single patient differed in order of development and severity, with papules, vesicles and pustules simultaneously present in the same patient.

Focal areas of necrosis, resembling the cutaneous pox, were seen in many viscera. The pleura and peritoneum were involved in all cases. Peritoneal lesions were often superficial and serosal lesions on the gastrointestinal tract were usually not associated with a mucosal defect. In contrast, pleural, splenic capsular and hepatic surface involvement was invariably associated with parenchymal destruction. Although the pleural or peritoneal lesion was covered by a layer of fibrin, generalized accumulation of fibrin or extensive amounts of free fluid was not observed.

The pulmonary changes included pleural, parenchymal, tracheobronchial and interstitial involvement. Hyperemia of alveolar septae and swelling of cellular elements was found. The alveoli contained large amounts of precipitated protein, often deposited against the alveolar wall similar to hyaline membrane disease.

Cardiovascular changes were usually limited to endothelial and muscular swelling in small arteries and veins. Occasionally, this process had progressed to frank necrosis. The spleen and lymph nodes were invariably moderately enlarged due to reactive hyperplasia. Oral mucosa contained pox in most cases and esophageal mucosa was involved in two cases. Hepatic foci of necrosis were usually seen in the parenchyma and showed no predisposition for a particular portion of the lobule.

Nervous system involvement was frequent. In half the cases, cerebral edema contributed to death. Meninges on gross examination were normal or showed only hyperemia. Microscopically, the subarachnoid space contained accumulations of lymphocytes, histiocytes and rare polymorphonuclear cells. Sections through the brain and spinal cord revealed striking edema.

Discussion

In reviewing the 20 cases, a pattern similar to the findings of varicella pneumonia as described by Southard²⁷ was noted. A typical adult case may be reconstructed as follows:

The onset is with fever, followed within 48 hours by skin rash and a dry harassing cough. The rash rapidly involves the oropharyngeal mucosa and the cough becomes productive of tenacious, blood-tinged sputum, coincident with chest pain, dyspnea, and cyanosis. On hospital admission the patient is found to be acutely ill, with fever, tachycardia and tachypnea. Sputum and blood cultures reveal no pathogens and all agglutination studies are negative. The leukocyte count is within normal limits without significant left shift of the differential count. An x-ray film of the chest on admission shows diffuse areas of fine, nodular infiltrations throughout both lung fields with a tendency toward confluency. Despite oxygen, supportive therapy and use of wide spectrum antibiotics, improvement is by lysis. A roentgenogram of the chest taken seven days after admission shows some clearing of the miliary pulmonary infiltration with further clearing by the tenth hospital day. One month later, the patient is symptom-free and no significant abnormality is noted on a pulmonary radiograph. This pattern seen in adults is in sharp contrast to the usually mild course of chickenpox in childhood.

In children, pneumonia is usually due to secondary bacterial infection with hemolytic staphylococcus aureus or streptococcus hemolyticus, rather than to the varicella virus itself. This latter may occur occasionally, as well as encephalitis and nephritis which may prove fatal. Waring and coworkers,³⁰ quoting Bullowa,⁵ said that the incidence of pneumonia in chickenpox is approximately 0.8 per cent as against 1.5 per cent in scarlet fever, 4.1 per cent in diphtheria, 12 per cent in measles and 19 per cent in pertussis. Empyema was more common after bacterial pneumonia complicating chickenpox (14 per cent) than after any other contagious disease except scarlet fever (36 per cent).

Two of the four children included here had manifestations of bacterial and viral complications. Viral pneumonia was documented histologically in addition to hemolytic staphylococcus septicemia and multiple abscesses. Widespread viral invasion of numerous organs of both children suggests decrease in host resistance. One child had no history suggesting increased susceptibility to viral or bacterial infections and had been successfully vaccinated against smallpox. He did not receive steroids. The second had known hypogammaglobulinemia but had received appropriate gamma globulin replacement therapy. Vaccination against

smallpox had been unsuccessfully administered. Steroids were used therapeutically. The documented hypogammaglobulinemia and decreased resistance to infection may have contributed to overwhelming bacterial invasion. The possibility of synergism between the combined viral and bacterial infections must be considered, irrespective of humoral factors.

This clinical impression is substantiated by laboratory demonstration of decidedly increased virulence of combined viral and bacterial infections.^{3,4,17} The mechanism is as yet undetermined but may be due to inhibition of natural bactericidal or bacteriostatic substances. The remaining two children had widespread viral, organ involvement without secondary bacterial infection and without evidence of immunologic paresis.

The direct relationship of severity of the rash to severity of the disease has been documented. Lack of constant correlation between physical findings and radiographs is indicated by absence of rales and normal breath sounds in five patients, in spite of abnormal pulmonary roentgenograms.

The roentgenographic findings, especially the nodulation, are not pathognomonic of varicella. However, the association with typical skin lesions offers sufficient evidence to establish a correct diagnosis. The appearance of the acute acinar nodulations occurs early in the course of the disease. Radiographic improvement lags behind the clinical recovery, which usually requires one to two weeks. Chemotherapy does not seem to affect the regression rate of roentgenographic changes.



Figure 2.—X-ray film of chest of same patient as in Figure 1 five years later, showing residual diffuse small fibronodular lesions.

The slow regression of pulmonary abnormalities, in some cases extending over two and a half months, suggests classification of the disease as a subacute or even chronic miliary process.¹⁰ Abrahams, and co-workers¹ and Knyvett¹⁹ have described some cases as falling into a chronic category. They found this to be a cause of pulmonary calcification and they emphasized that it must be included with tuberculosis and histoplasmosis as a cause of multiple nodular pulmonary calcifications. Follow-up films on nine of the cases in the present series, taken as long as five years after the initial infection, have not shown calcifications. Six of the nine patients did have residual fibrotic nodulations at the lung bases (Figure 2).

Secondary pulmonary invasion by pathogenic bacteria in patients with chickenpox but without viral pneumonia can cause radiographically similar bronchopneumonia. However, bacterial pneumonia usually has a more patchy distribution course, hilar bronchial infiltration and lobar or segmental consolidation. There is usually associated leukocytosis with a shift of differential to the left. Blood and sputum cultures may reveal the causative organism and it usually appears later in the course of the disease than is the case with viral pneumonia,¹⁶ especially in children. Occasionally, transient, mild cardiac enlargement has been reported early in the disease.^{14,30} Other complications include pulmonary edema, mediastinal and subcutaneous emphysema and pleural effusion.

Therapy was applied in different ways. Those patients with very mild to moderate illness were given only symptomatic and supportive treatment. The three patients in this group made rapid recovery without difficulty. There were no complications and pulmonary abnormalities cleared spontaneously even though hemoptysis was present in one patient.

The remaining 17, who were obviously more severely ill, were given intensive therapy with oxygen and antibiotics, and some of them also received adrenal steroid therapy. It is generally agreed that the value of antibacterial drugs is limited to treatment of secondary bacterial infection.²¹ Adrenal cortical steroids have been advocated as anti-inflammatory agents to reduce alveolar exudate and septal edema, thus facilitating pulmonary gaseous exchange. Their value has been recognized^{15,16,21} in association with certain viral infections but the literature contains conflict-

TABLE 2.—*Post Mortem Distribution of Lesions by Organ System*

| <i>Case</i> | <i>1 (54 Years)</i> | <i>2 (35 Years)</i> | <i>3 (4 Years)</i> | <i>4 (6 Years)</i> | <i>5 (2-7/12 Years)</i> | <i>6 (3 Years)</i> |
|-------------------|-----------------------------------------------|--------------------------------------------------------------------------|------------------------------------------------|-------------------------------------------------------------------------------------|--------------------------------------|-------------------------------------------------------|
| SKIN | Face, Chest, Arms | Head, Neck, Chest, Thighs | Face, Chest, Arms | Face, Chest, Arms Lower Extremities | Face, Chest, Back Oral Mucosa | Trunk, Arms, Legs |
| MUSCULO-SKELETAL | | | Osteomyelitis | | | |
| RESPIRATORY | Pleural pox, Pneumonia | Pleural pox, Pulmonary edema, Tracheal ulceration, Hemorrhagic pneumonia | Pleural pox, pneumonia | Pleural and tracheal pox, Pulm. infarct., Hyaline membrane, Interstit. pneumothorax | Pleural pox, Pneumonia | Pleural pox, Tracheal pox, Inclusions, Pneumonia |
| CARDIO-VASCULAR | | | Myocardial abscess | | | Epicardial pox |
| HEMIS & LYMPHATIC | | | | Splenic pox Reactive hyperplasia | Splenic pox, Node necrosis | Splenic necrosis and infarction, Reactive hyperplasia |
| DIGESTIVE | Peritoneum pox, Liver pox | Esophagus pox, Liver pox, Necrosis peritoneum | Liver pox, Esophagus pox, Peritoneum pox. | Liver pox on capsule, Areas of necrosis peritoneum | Esophagus pox, Liver necrosis | Liver subcapsular necrosis, Peritoneum |
| UROGENITAL | | Left ovarian pox | | | | |
| ENDOCRINE | | | | | | |
| NERVOUS | Petechial midbrain hemorrhage, cerebral edema | | Cerebral edema, Perivascular cuffing | | Edema, Microgliosis pus satellitosis | Perivascular lymph nodes, Edema of brain and cord |
| CAUSE OF DEATH | Varicella pneumonia. Cerebral edema. | Varicella pneumonia. | Varicella pneumonia, Staphylococcal septicemia | Respiratory inadequacy, Cerebral edema, Varicella encephalitis. | Varicella pneumonia. Cerebral edema. | Cerebral edema, Varicella encephalitis. |

ing opinions relative to their value in varicella pneumonia. Reports of single patients successfully so treated have been presented by several authors.* A series of 15 patients treated in this manner, without a death, is reported by Bower.³ Controlled studies are few, but one recent study reports no difference between steroid treated patients and controls.²³

Of the 11 moderately to seriously ill patients (category 2, as described earlier) treated with antibiotics and oxygen in the present series, four died within 26 hours after admission. Severe alveolar-capillary block was the cause of death in one patient but in the other three the immediate cause of death was meningoencephalitis with respiratory depression, midbrain hemorrhage with cardiac arrest and staphylococcal septicemia. In the group of six moderately to extremely ill patients (category 3) treated with antibiotics, oxygen and adrenal steroids, two died. One died of alveolar-capillary block and hepatitis but the other had multiple complications and death was primarily due to meningoencephalitis and staphylococcal septicemia.

The high proportion of deaths due to severe extrapulmonary complications suggests the necessity of very careful evaluation of possible extrapulmonary disease in each case of varicella pneumonia. Adult patients with mild to moderate varicella pneumonia do not usually have complicating bacterial infection, and antibiotics therefore usually add nothing to their therapy. Younger children are more likely to have serious secondary bacterial infection than adults. Clinical and radiographic examination cannot always differentiate viral from bacterial pneumonitis, and overwhelming staphylococcal septicemia may be accompanied by leukopenia. In seriously ill pediatric patients, antibiotic therapy is indicated initially until available cultures can determine whether or not it is needed. In the present series, adrenal cortical hormone therapy was not associated with any significant improvement in the condition of the patients.

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Hyperglycemia During Intravenous Fluid Therapy

A Clue to the Presence of Diabetes Mellitus

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■ *Twenty-two patients receiving 5 per cent glucose solution intravenously during an acute illness were studied for evidence of hyperglycemia. Those in whom blood sugar rose above 100 mg per 100 ml (Folin-Wu) during intravenous therapy subsequently had impairment of carbohydrate tolerance as measured by oral glucose tolerance tests. The data collected suggested that blood sugar of 100 mg per 100 ml (Folin-Wu) or more developing in such a setting is a clue to the presence of diabetes mellitus.*

THE DEVELOPMENT OF hyperglycemia in patients receiving glucose-containing solutions intravenously during treatment of an acute illness is not uncommon. This finding is often casually dismissed by physicians as reflecting nothing more than the fact that the patient is receiving a large load of sugar and his system temporarily "saturated." Hyperglycemia in such circumstances is rarely regarded as an indication that diabetes mellitus may be present.

In contrast with this belief, recent work has shown that metabolically normal persons can tolerate large loads of intravenously administered glucose without deviation of the blood sugar to above-normal levels. Seltzer and Harris¹ gave 3,000 ml to 4,000 ml of 15 per cent glucose solution daily for five to seven days to normal persons and obtained mean blood sugar below 100 mg per 100 ml during the entire experiment in spite of a concurrent additional oral load of 220 to 300 gm of carbohydrate per day. This tolerance of continued and severe hyperglycemic stress dif-

ferentiated the normal persons from tolbutamide-sensitive diabetic or insulin-dependent diabetic persons, in whom hyperglycemia and glycosuria did develop under similar glucose intake (see Chart 1.).

This data strongly supports the concept that the hyperglycemia which develops under intravenous glucose loading is an abnormality of a magnitude proportional to the basic physiologic impairment. However, the clinical value of Seltzer and Harris' study to the physician at the bedside is limited by the fact that 15 per cent glucose solutions are rarely, if ever, used to treat patients. Also, in the usual clinical situation the oral intake of patients who are being treated parenterally is usually quite restricted. Furthermore, acutely ill patients are under severe metabolic stress with increased adrenocortical activity which tends to promote the development of hyperglycemia, in contrast to the stable situation described in the Seltzer and Harris experiment. These facts suggested the desirability of determining whether hyperglycemia noted during treatment with the usual intravenous glucose-containing solutions in

Submitted 9 March 1967.

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a clinical setting has a similar value as a clue to the presence of diabetes.

Materials and Methods

Acutely ill patients admitted to the Medical Service of the hospital were selected for inclusion in the study on the basis of the following criteria: (1) Presence of a disease requiring at least three days of intravenous fluid therapy which included 2,500 to 3,000 ml of 5 per cent glucose per 24 hours. (2) Absence of acute pancreatitis, wasting disease, malnutrition or known diabetes mellitus. (3) Absence of endocrinopathy or treatment with corticosteroids. (4) No recent or on-going treatment with thiazide diuretics. (5) Expectation of survival.

No attempt was made to alter the course of treatment undertaken by the house staff and attending physicians.

Blood sugar levels were determined (Folin-Wu method) twice daily, at 8:00 a.m. and 3:00 p.m.: The specimens were obtained from a vein in an extremity not being used for infusion and were drawn while the patient was receiving parenteral fluids. In our laboratory this method yields results which average about 20 mg per 100 ml above those obtained with the Somogyi-Nelson (true glucose) method. All fluid intake and output was carefully recorded.

During convalescence, and at least two weeks after the acute phase of illness, each patient was given a diet providing 250 gm of carbohydrate per day, and a standard three-hour glucose tolerance test (SGTT) was performed three days later. Certain patients who had elevation of blood sugar during intravenous therapy or who had borderline standard glucose tolerance were further evaluated by the performance of a cortisone-glucose tolerance test.

Results

Forty patients were studied in a period of eight months. Clinical data about 22 are listed in Table 1. The others were dropped from the study because of death, insufficient fluid administration or inadequate data.

Despite the interest and cooperation of nursing staff and house officers, not all blood sugar determinations ordered were obtained: occasionally infusions were interrupted by blood transfusions, or had been stopped at the time blood specimens were to be drawn.

To evaluate results, the values given by Conn and Fajans for the standard glucose tolerance curve were increased by 20 mg per 100 ml and the curves interpreted by the values given in Table 2.

Except for patient 7, all patients in the normal group had blood sugar consistently below 120 mg per 100 ml and their overall mean blood sugar for all five days remained below 100 mg per cent. This compares with levels as high as 260 mg per 100 ml in those who later were found to have clearly diabetic glucose tolerance curves, and whose overall mean blood sugar was 122 mg per 100 ml for the five days of study. It was also interesting that patients whose standard glucose tolerance test was only suggestive of pre-diabetic state had an overall mean blood sugar slightly higher than the clearly diabetic patients. However, the difference is probably not statistically significant. These patients are classified as probable pre-dia-

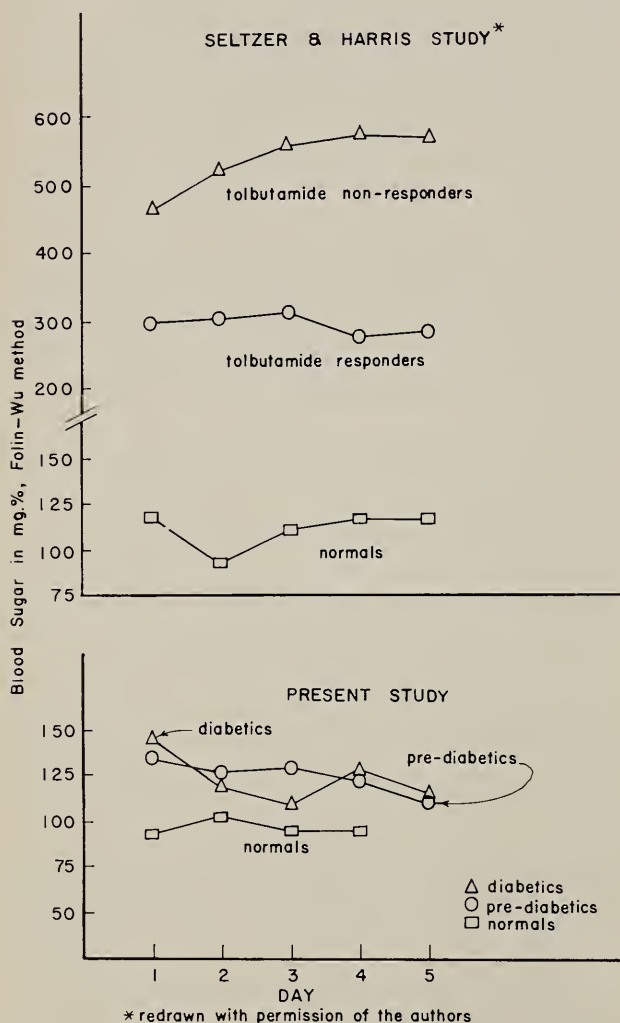


Chart 1.—Mean daily blood sugar values during intravenous glucose infusion: comparison of Seltzer and Harris experiment with present study.

TABLE 1.—Venous Blood Sugar (mg per 100 ml, Folin-Wu Method)

| Non-Diabetic Patients | | | | Number of Determinations | | | | |
|-------------------------------------------|-----|-----|--------------------------------------|--------------------------|------|------|------|------|
| Patient | Sex | Age | Diagnosis | 1 | 2 | 3 | 4 | 5 |
| 1 | F | 77 | Congestive failure | | 114 | | | |
| 2 | M | 45 | Esophagitis | | | 116 | | |
| 3 | F | 47 | Obesity | 108 | 87 | 84 | 110 | 100 |
| 4 | M | 24 | Chronic myelogenous leukemia..... | | 90 | 69 | 80 | |
| | | | | | | 68 | | |
| 5 | M | 49 | Chronic lymph. leukemia..... | 89 | 74 | | | |
| 6 | M | 89 | Senile dementia..... | 89 | 106 | 115 | | |
| | | | | 97 | 115 | 109 | | |
| 7 | M | 17 | Peptic ulcer | | 131 | 105 | | |
| | | | | | 100 | 97 | 92 | |
| | | | MEAN..... | 94 | 102 | 94 | 94 | |
| | | | SD | 11 | 25 | 19 | 15 | |
| Overall Mean = 96 mg per ml (4 days only) | | | | | | | | |
| Diabetic Patients | | | | | | | | |
| 8 | M | 82 | Bronchopneumonia | 254 | | 260 | | |
| 9 | M | 50 | Stroke | 105 | | | 169 | |
| 10 | M | 85 | Pyloric obstruction | 130 | 114 | | 130 | |
| 11 | M | 49 | Peptic ulcer | | 126 | 156 | 156 | 104 |
| | | | | | | | | 104 |
| 12 | M | 37 | Peptic ulcer | 155 | 122 | 97 | 122 | |
| | | | | 110 | 105 | 100 | 110 | |
| 13 | M | 34 | Mitral stenosis | | 122 | 85 | 97 | |
| 14 | M | 70 | Emphysema | | 110 | 100 | 102 | |
| 15 | M | 65 | Stroke | 122 | 102 | | | |
| | | | | 110 | 120 | 126 | 164 | 138 |
| 16 | F | 26 | Scarlet fever | 156 | 142 | 131 | 164 | |
| | | | | | | 100 | 92 | |
| 17 | F | 80 | Angina, ileus | | 124 | | 100 | |
| | | | | | 132 | 118 | 97 | |
| | | | MEAN..... | 142 | 120 | 112 | 125 | 115 |
| | | | SD | 49 | 11.5 | 57 | 30 | 18 |
| Overall Mean = 122 mg per ml | | | | | | | | |
| Pre-Diabetic Patients | | | | | | | | |
| 18 | M | 61 | Cirrhosis, Rheumatoid arthritis..... | 147 | 110 | 184 | 143 | |
| | | | | | | 136 | 110 | |
| 19 | F | 17 | Trauma | | 165 | 140 | 160 | |
| 20 | M | 59 | Adynamic ileus | 126 | 88 | 100 | 122 | |
| 21 | M | 64 | Bronchopneumonia | | 114 | | 122 | 94 |
| | | | | | | | 87 | |
| 22 | F | 62 | Hiatus hernia | | 156 | 92 | 102 | 114 |
| | | | | | | | | 126 |
| | | | | | | | | 116 |
| | | | MEAN..... | 136 | 126 | 130 | 121 | 112 |
| | | | SD | 15 | 32 | 37 | 25 | 14 |
| Overall Mean = 125 mg per 100 ml | | | | | | | | |

TABLE 2.—Criteria for Interpretation of Glucose Tolerance Test (Venous Blood, Folin-Wu Method, in mg per 100 ml)

| Time | Normal | Diabetic | Probable Diabetic |
|---------------|---------------|---------------|-------------------|
| Fasting | Less than 120 | | |
| Post Prandial | | | |
| ½ hour | Less than 180 | | |
| 1 hour | Less than 180 | More than 180 | More than 180 |
| 2 hours | Less than 130 | More than 140 | 130 - 140 |

betics on the basis of subsequent grossly abnormal cortisone-glucose tolerance tests.

Statistical analysis of the data does suggest, however, that the values obtained for the three groups of patients that were classified as normal, diabetic and pre-diabetic on the basis of the SGTT or CRTT, probably represent samples from three distinct populations. Analysis of variance for a single measurement variable was applied. A 99 per cent level of significance was chosen to test the hypothesis that the data do not represent samples from three statistically different populations. Although the samples evaluated are small, and therefore the variances, as estimated by the standard deviations obtained, are not clearly homogeneous, the results of the analysis are changed very little by assuming normal distribution and equal variance.⁴

On the basis of results of statistical analysis, the hypothesis was rejected.

Comments

These findings suggest that a metabolically normal person receiving the usual therapeutic quan-

ties of glucose-containing parenteral fluids will remain euglycemic, even under the stress of severe illness and the added handicap of age. This means a true blood sugar level of about 80 mg per 100 ml, a conclusion consistent with the findings of Seltzer and Harris. It appears reasonable, therefore, to suggest that a patient with a blood sugar (Folin-Wu) of 100 mg per 100 ml or above under the circumstances described is likely to be diabetic and deserves a glucose tolerance test to rule out the presence of diabetes mellitus. A patient whose SGTT is borderline should undergo further study by way of a CGTT.

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Suicides in San Mateo County

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■ *The usual surveys of completed suicides, encompassing, as they do, large geographical areas, are of limited value to physicians of a particular community. The unique and differentiating characteristics of the suicides in his locale may be "washed out" in these large surveys.*

San Mateo County has an annual suicide rate of 17 per 100,000 and a disproportionately high incidence in persons over 65 years old. In this particular county females, widows and Orientals are more prone to suicide than has usually been reported elsewhere. Alcohol was directly or indirectly involved in a significant number of instances. Many of the persons who killed themselves were under a physician's care at the time of self-destruction.

There are probably important ecological and sociological variables as well as personal factors involved in the suicidal process that are of significance to any suicide prevention program. It is urged that there be more extensive and comparative research in this important public health problem.

EACH YEAR IN California more than three thousand persons kill themselves and our state's annual rate of 17 per 100,000 population is one of the highest in the country.² Since regularity of this phenomenon year after year eliminates the possibility that this tragic situation is merely the result of chance, more intensive efforts at prevention are called for.

One approach to prevention has been a statistical analysis of the completed suicides to identify the high-risk persons, the precipitating stresses, and the more commonly used methods of self-destruction. It is hoped that the findings of such analyses would aid the practicing physician in the recognition and management of such patients. Were it possible for the physician to have more reliable indicators of who is the potentially suicidal person, he could institute more vigorously the necessary treatments and required precautions.

However, most such surveys and analyses have covered large geographical units, such as countries and states. Since the frequency and methods of suicide vary widely from state to state and even in different areas of large cities, the results of such surveys produce averages and stereotypes that are of limited usefulness to the practitioner of a particular community or county. In fact, such large studies encompassing extensive areas and populations may mask or "wash-out" significant differences between the smaller geographic units and populations.

The health departments of each county faithfully publish periodic reports of the local epidemiological characteristics of such illnesses as tuberculosis, poliomyelitis and peptic ulcer; yet suicide, the ninth most common cause of death—far more common than the diseases mentioned and a more serious public health problem—receives relatively little attention. In fact, there is much evidence that the official statistics significantly understate the actual toll.

Submitted 28 December 1966.
Reprint requests to: Veterans Administration Hospital, 3801 Junipero Serra Blvd., Palo Alto 94304.

Method of Study

In an effort to develop more specific data regarding some aspects of the suicide problem in San Mateo county, we have done an analysis of all the suicides in our county during the five-year period 1961 through 1965. Available to us for each case were reports, in varying degrees of completeness, by police and deputy coroners, as well as interviews with members of the suicides' families, friends and employers, letters from physicians, notes left by the suicides, autopsy and toxicological findings. We focused particularly on the kind of information that might be easily available to the busy physician. Although such records, because of family distortions and concealments, have many limitations in understanding and evaluating the suicide process, nevertheless they do constitute a valuable initial point of reference.

Findings

Incidence: The number of suicides per year ranged from a low of 77 to a high of 83 and the average was 80. Since the population of the county during this period has been estimated to be 488,000, the annual rate is 17 per 100,000. This rate is significantly above the overall United States figure of 11, but is equal to the California rate of 17. Stated somewhat differently, 4 per cent of the deaths in this county are by suicide.

Age. Most of the suicides were in the age range of 30 to 60, but since that is the largest population group at risk, this finding is not surprising. However, the significant relationship between suicide and the older age group is indicated by the fact that although persons over 65 years represent only 7 per cent of the population, 21 per cent of the suicides are in that group.

Sex. Sixty-six per cent of the group were males, the male to female ratio being 2:1. Since the disparity is somewhat less than the national ratio of 3:1, it suggests that in this county women are more prone to suicide than women in other areas.

Race. In a community where 95 per cent of the population is white, it is not surprising that suicide by a non-Caucasian is rare. However, the predisposition of Orientals to suicide is indicated by the fact that although they represent only 1.3 per cent of the population, they make up five per cent of the suicides.

Marital status. In both sexes approximately 50 per cent of the suicides were married and 16 per

cent were either divorced or separated at the time of death. Widows constituted 15 per cent of the suicides, but the comparable figure in widowers was only 5 per cent, suggesting that males better tolerate the loss of their marital partners. On the other hand, 8 per cent of the male suicides were single, but there were no known single females who killed themselves. Perhaps females tolerate the unmarried state better than males.

Method. Eighty three per cent of the suicides were done by one or another of four methods: 32 per cent were by gunshot (chiefly males), 22 per cent by drugs (chiefly women), 17 per cent by carbon monoxide and 12 per cent by hanging. The remainder were by rare and miscellaneous methods such as slashing the throat and jumping from high places. Interestingly—and reflecting the local variations of the problem—suicide by jumping from heights made up only 1 per cent in this county whereas in the adjacent San Francisco county with its high bridges and buildings, it constitutes 10 per cent.

The proportion of suicides by carbon monoxide was surprisingly high. In most previous surveys, suicide by running an automobile engine in a closed garage or piping the exhaust into the interior of a car was found to be rare.

In those instances where drugs were the means of suicide, the drugs used were either sedatives, hypnotics or tranquilizers. Often several drugs were taken simultaneously. One of the more regrettable aspects of this situation is that the drugs had been prescribed by a physician.

Alcohol. The significance of alcohol is indicated by the fact that, regardless of the primary method of suicide used, at postmortem 21 per cent of the male suicides and 9 per cent of the female suicides had blood alcohol above 0.05 per cent. In most instances the drinking preceding death seemingly was merely the continuation of a long-standing behavior pattern rather than an effort to reduce the dread of committing the suicidal act.

Previous Contacts with Physicians. Our findings were similar to those reported by Motto and Litman.^{5,6} The records indicated that at least 37 per cent of the suicides had consulted a physician within the six months preceding the suicide; in a significant proportion within the last month of life.

These physicians ranged from general practitioners to specialists. While in some instances the presenting symptoms were suicidal feelings, many

were of some "somatic mask" of depression or were cryptic cries for help in dealing with a sense of hopelessness and despair.³

In half of these cases in which there had been a relatively recent medical contact, the physician was a psychiatrist. While this is to be expected to some extent in light of the skewed nature of the group of patients being reviewed, nevertheless it emphasizes that even among psychiatrists there is a need for improved ability to accurately assess the suicidal potential.⁴

Motivation. The loss of life by suicide is a tragedy in any circumstances, but in view of theories of its relationship to social disorganization, it is particularly perplexing and disturbing that it should occur in a county with all the advantages of San Mateo. This is one of the ten most well-to-do suburban residential counties in the United States (median family income of \$8,103¹). Housing for the most part is high-cost and in good condition. The median education is 12.4 completed years of schooling, which is comparatively high.

The population is relatively youthful, is rapidly increasing in size and is made up of an unusually large number of professional and managerial personnel. The year-round climate is mild, pleasant and without extremes. The Peninsula is a nationally recognized educational and cultural center and is the location of many firms active in the research and development of the aerospace and electronics industries.

Perhaps suicide is a disease particularly of such affluent areas. Some other suggestive clues to the problem are a very high divorce rate and an influx of large numbers of people from other localities, with concomitant poor family and group ties.

Retrospective determination of the suicides' possible motivations to die obviously has many potential errors. However, based on the surprisingly large amount of information available to us, it was possible to make tentative conclusions regarding the precipitating stresses in most instances.

Discouragement over mental illness, such as a psychotic relapse or a deepening of an endogenous depression, seemed to be the primary stress in 25 per cent of cases. Marital difficulties and concern over physical ill-health each appeared responsible for the suicide in 14 per cent. Other significant motives were bereavement, alcoholism, business difficulties and unemployment. Despite our efforts, the motive could not be ascertained in a large number of cases.

Discussion

From this limited attempt to describe the characteristics of some aspects of the suicide problem in one county, it becomes apparent that we need to develop much more information in order to improve our understanding of suicide and our suicide prevention programs. In addition, comparative studies between San Mateo and other counties might isolate significant ecological and sociological clues to the problem. Probably in the future we will have available computer techniques to permit us to analyze in greater depth and breadth the possible factors involved in this long-neglected serious public health problem.

Acknowledgement

We wish to express our sincere appreciation to the coroner of San Mateo county, Mr. Paul B. Jensen, and his staff for their valuable assistance in this research.

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The Treatment of Nevus Cell Nevi (Pigmented Nevi)

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■ *There are four reasons for treating nevus cell nevi (moles): (1) The prevention of malignant change; (2) malignant change already present; (3) cosmetic improvement; and (4) anatomical or functional changes.*

Complete removal of the lesion is essential for the former two indications, but partial removal is sometimes all that is necessary for the latter two. Pathological examination is mandatory, no matter which method of removal is used.

THE NEVUS CELL nevus is the most common tumor of the skin, occurring in all people at an average of 20 nevi per person.^{11,12} As this is a common and noticeable tumor, and as the malignant melanoma develops from the nevus cell nevus in the majority if not all instances, it is obvious that the management of nevi is the concern of all physicians and many patients. Fortunately, only about one in every million nevi becomes malignant.¹¹

The treatment of nevi has been greatly influenced by traditional teaching based on little, if any, scientific evidence. For example, trauma, acute or chronic, either accidentally or surgically produced, has been blamed for the stimulation of malignant change in benign nevi. There is no documented evidence that a previously treated histologically proved benign nevus cell nevus has become malignant following trauma of any type. In fact, the evidence that is available concerning the changes that occur in pigmented nevi following partial removal and electrodesiccation with histological observation before and after tends to show that malignant transformation does not occur.^{14,6,7}

Also, incisional methods of biopsy of pigmented tumors suspected of being malignant melanoma have been considered hazardous because of the general belief that cutting into them increases the tendency to lymphatic or hematogenous spread of malignant cells. Again, there is no documented statistical proof that this occurs. Even a limited excision (that is, an excisional biopsy) of a malignant lesion does often pass through cancer-bearing tissue (as is sometimes proved by local recurrences of malignant melanoma) and, if the theoretical objection to an incisional biopsy exists, then it should also apply to limited local excisional biopsy.¹⁰ In these circumstances, shave biopsy and electrodesiccation might be a preferable method of partial biopsy because of the resultant sealing off of lymphatic and blood vessels. Also, there is no evidence that the inflammation or ulceration of a melanoma resulting from trauma accelerates the growth of the lesion.¹

There are four indications for the treatment of nevus cell nevi. First, the possibility of malignant change occurring in a nevus sometime in the future (a pre-malignant active junctional nevus) and treatment is prophylactic as well as diagnostic; second, a suspected malignant change already present, and treatment is again diagnostic and therapeutic; third, cosmetic reasons; fourth, functional and ana-

Submitted 17 February 1967.

Originally presented before the Section on Dermatology at the 95th Annual Session of the California Medical Association, Los Angeles, 19 to 23 March 1966.

Reprint requests to: Department of Dermatology, Stanford Medical Center, 300 Pasteur Drive, Palo Alto 94304 (Dr. Walton).

tomical changes occurring in a nevus. The latter reasons, including irritation, trauma and infection, do not predispose nevi to malignant change, but removal is often advisable because of the associated nuisance and discomfort. This is particularly true with nevi in certain areas that are recurrently or chronically subjected to these changes, such as the intertriginous areas, the hairy areas and pressure points under articles of clothing. Hairy nevi can also be subjected to painful subneval folliculitis, which is often a recurrent and annoying problem.

The method of treatment of pigmented nevi not only depends upon the indication for removal, but also the size, the clinical and morphological type, the location and the age of the patient. Even in the best circumstances of clinical evaluation of nevi by experts, it is very evident that clinical acumen is not sufficient, and pathological examination of all treated nevi is mandatory.^{13,4} In either of the first two categories, there is a possibility of malignant or pre-malignant change occurring; and complete removal or destruction of the nevus is therefore essential. Any method of treatment may be adopted whereby an adequate biopsy specimen is obtained and the residual nevus cells completely removed or destroyed at the time or in the immediate future. Usually, if the lesion is not too large, simple elliptical excision with primary closure of the wound is the treatment of choice.

In contradistinction, treatment of nevus cell nevi for cosmetic or functional reasons does not always necessitate complete removal or destruction of all nevus cells. Very often, the best result is produced by shaving off the nevus flush with the skin and then gently electrodesiccating the base. However, many physicians assume that, because the nevus has been removed for cosmetic or functional purposes, electrodesiccating or other similar treatment of physical type is always the method of choice. Possibly because of a lack of training or inclination, surgical excision is often neglected when it is the best form of treatment irrespective of the type of nevus or the reason for removal.

The morphology of benign nevus cell nevi influences the choice of method of removal. A good example is the blue nevus, in which the nevus cells are located deep in the dermis and, therefore, a pitted scar is left if the lesion is removed by shave excision and electrodesiccation. It is sometimes difficult to differentiate blue nevus clinically from a malignant melanoma, and excisional biopsy is the best form of treatment.

The hairy pigmented nevus is another example of how gross structure can influence the method of treatment. Even though hairs can first be removed by electrolysis and then later the residual lesion removed by shave excision and electrodesiccation (or comparable methods), it is often simpler to excise the lesion in the first place, thereby producing an equally good cosmetic result. In order to carry out partial shave excision and electrodesiccation and achieve the best result, a lesion should usually have elevation to it; and flat nevi therefore often lend themselves far better to simple excisional biopsy.

The size of nevi is a factor in the choice of treatment. Medium to large nevi are a particular problem, and except for the premalignant active junctional type, are best removed by shave excision and electrodesiccation, or sometimes by piecemeal excisional procedure. Both methods produce a better cosmetic result than reconstructive operation and skin grafting. However, the latter method may be the only one available in the case of very large nevi, such as the bathing trunk type.

Location of the nevus can be a determining factor in the method of removal. Surgical excision of lesions on the back often produces a scar which spreads and is quite unsightly. The same lesion can be removed by shave excision and electrodesiccation with a resultant soft, pliable, smaller scar which does not stretch and usually improves with age. Shave excision and electrodesiccation is the treatment of choice of nevi on the eyebrow, as excisional surgery will remove the hair follicles, thereby reducing or even completely destroying part of the eyebrow. For similar reasons, large nevi on the scalp are better treated by shave excision and electrodesiccation.

The controversy regarding whether nevi on the hands and feet and genitalia should be removed prophylactically still exists. The argument in favor of removal is based on information that shows that the majority, if not all, nevi in these areas are of the true junctional type; and although the hands and feet only constitute 10.5 per cent of the body's skin surface, nevertheless approximately 16.5 per cent of melanomas occur in these areas, and of these 80 per cent are on the feet.^{5,1} This point of view is countered by the various clinical studies showing that approximately one in every six persons has at least one nevus on the palm or sole, and therefore prophylactic extirpation of such lesions would be physically impossible.^{15,8,2}

Subungual nevi appear to be rare. In one investigation no nevi were found in a thousand persons studied; but the subungual melanoma does constitute 3.3 per cent of all melanomas.^{2,3} Therefore, a subungual pigmented tumor, unless it is obviously due to a benign condition such as a wart or subungual hematoma, should always be excised because of the possibility of its being a malignant melanoma.

Comment

All nevi removed should be pathologically examined to determine the type of nevus. Occasionally, clinical errors are made, and if the lesion proves to be a malignant melanoma or a premalignant junctional nevus, then the area can be re-excised widely without affecting the ultimate prognosis.^{13,4} Junctional changes are obviously not in themselves a reason for re-excision, as most nevi, even those that are clinically obviously intradermal in nature, contain some junctional changes.⁹ We have found, from our previous investigations, that usually within one year following partial excision and electrodesiccation of nevi, there is increased junctional activity and pigment formation. Our work so far shows that these changes usually decrease after one year. The clinical importance of this is that sometimes pigment reforms at the site of removal, and that in time may get less or even disappear.¹⁴ If this recurrence of pigment is unsightly or unacceptable to the patient, it can again be removed by shave excision and electrodesiccation. The occurrence of this pigment is fairly common, and its presence should not be, in itself, a sign for wide surgical excision of the area. It occurs more commonly in younger persons and in the more darkly pigmented lesions, and again in lesions which pathologically prove to have a good deal of junctional activity. To avoid recurrence of the pigmented lesions in such individuals, surgical elliptical excision is often the treatment of choice rather than shave excision and electrodesiccation.

Conclusions

Partial removal of pigmented nevi by shave excision and electrodesiccation (or similar methods), accompanied by pathological examination, is the treatment of choice for certain benign nevus cell nevi, depending on morphologic features, size, and location. Active junctional nevi and suspected malignant melanoma should be removed in their entirety, preferably by excisional operation.

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ABNORMALITIES OF THE PLACENTA & NEWBORN INFANT










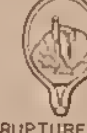





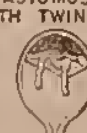






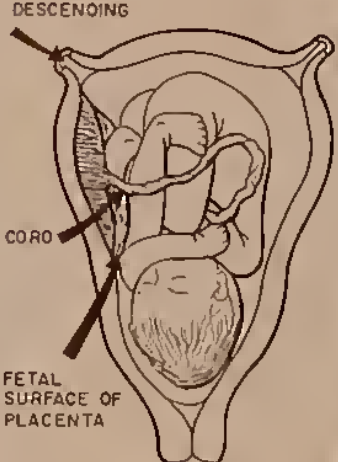
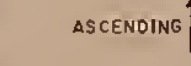












W. B. SCHAFER, M.D. & M. G. WILSON, M.D.

AMERICAN ACADEMY OF PEDIATRICS
CALIFORNIA CHAPTER, SECTION 2
FETUS AND NEWBORN COMMITTEE

The purpose of this poster is to serve as a brief reference and reminder for physicians and nurses of some of the conditions in newborn infants that occur with placental abnormalities. It is designed for the professional staff who care for obstetrical and newly born patients. More extensive information to supplement that given here is contained in the article from which the poster is derived: Wilson, M. G.: Placental abnormalities and fetal disease. Amer. J. Dis. Child. 108:154, August 1964.

The medical illustration was done by Mrs. Linda Dummel.

IF THESE PLACENTAL DISORDERS OCCUR, LOOK FOR THE FOLLOWING IN THE INFANT

| INTERFERENCE WITH FETAL CIRCULATION | | HEMORRHAGE WITH FETAL BLOOD LOSS | | MATERNAL-FETAL TRANSFUSION | TUMOR | AMNION NOOSUM | SINGLE UMBILICAL ARTERY | INTRAUTERINE INFECTION | PHYSIOLOGIC DISORDER |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>PLACENTA PRAEVI</p>  <p>ABRUPTIO PLACENTAE</p>  <p>PROLAPSE OF CORD</p>  <p>LONG CORD AROUND NECK</p>  | <p>CORO: KNOT, TORSION, STRICTURE</p>  <p>SHORT CORD</p>  <p>ENTWINE CORDS OF SINGLE OVUM TWINS</p>  <p>TUMOR OF CORD</p>  | <p>PLACENTA PRAE-VIA</p>  <p>CAESARIAN WITH ANT PLACENTA</p>  <p>RUPTURED PLAC. VESSEL OR VARIX</p>  <p>ABRUPTIO PLACENTAE</p>  | <p>VASA PRAE-VIA</p>  <p>RUPTURED VESSEL OF CORD</p>  <p>HEMORRHAGE INTO MOTHER, OR INTO PLACENTA</p>  <p>VASCULAR ANASTOMOSIS WITH TWINS</p>  |  | <p>TUMOR</p> <p>CHORIONEPITHELIOMA ①</p>  <p>CHORIO-ANGIOMA ②</p>  <p>METASTASES FROM MATERNAL</p> <p>MALIGNANT MELANOMA ③</p> <p>LYMPHOSARCOMA ④</p> <p>CARCINOMA OF LIVER ⑤</p> <p>FROM FETAL NEUROBLASTOMA ⑥</p>  |  | <p>SINGLE UMBILICAL ARTERY</p> <p>THE FOLLOWING MAY BE PRESENT</p> <ul style="list-style-type: none"> • ABNORMAL CORD LENGTH • VELAMENTOUS CORD • CIRCUMVALLATE PLACENTA • PLACENTAL INFARCTIONS  | <p>INTRAUTERINE INFECTION</p> <p>DESCENDING</p>  <p>FETAL SURFACE OF PLACENTA</p> <p>ASCENDING</p>  | <p>PHYSIOLOGIC DISORDER</p> <p>1 HYOROPIC ERYTHROBLASTOSIS</p> <p>IMMATURE EOEMA</p>  <p>2 DIABETES</p> <p>IMMATURE</p>  <p>3 TOXEMIA</p> <p>DEGENERATION INFARCTION</p>  <p>4 POSTMATURITY- DYSMATURITY</p> <p>DEGENERATION INFARCTION</p>  |
| <p>FETAL HYPOXIA & DISTRESS</p>  | | <p>ANEMIA, SHOCK, OR DEATH</p>  | | <p>POLYCYTHEMIA, PLETHORA, LETHARGY, CYANOSIS, AND CONVULSIONS</p>  | <p>METASTASES, MALFORMATION, HEMANGIOMA AND FETAL HYPOXIA</p>  | <p>ABNORMAL EARS, HYPOPLASTIC LUNG, KIDNEY- ABSENCE OF OR POLYCYSTIC, URETHRAL OBSTRUCTION, EDUINOVARUS AND STILLBIRTH</p>  | <p>HYDROCEPHALY, ANENCEPHALY, ABNORMAL EARS, ESOPHAGEAL ATRESIA, CONGENITAL HEART, KIDNEY-ABSENCE OF OR POLYCYSTIC, EXOMPHALOS, SPINE ANOMALY, IMPERFORATE ANUS, TRISOMY O OR E & STILLBIRTH</p>  | <p>INFECTION - JAUNOICE, LETHARGY, PNEUMONIA, AND CONVULSIONS</p>  | <p>1. HYOROPS 2.-3. NEONATAL OISTRESS 4. MALNUTRITION</p>  |

Government Regulations and the Use of Drugs

JOSEPH H. HAFKENSCHIEL, M.D., *Palo Alto*

■ *I have tried to trace the new drug development pattern from 1766, when Withering obtained his medical degree, to the present.*

The role of governmental authority as defined by the 1962 Kefauver-Harris amendments to the 1906 law and the subsequently issued regulations has been summarized. Four phases of testing in man have been detailed.

Something of the scientific or research capability of the pharmaceutical industry has been presented.

It is concluded that in the period of over two hundred years of medical education in the United States, the university hospital has become more and more the focus of medical research, teaching and practice in the community. The safety and effectiveness in the use of drugs in the future will depend upon the liaison and rapport of the industry physicians, government officials and the university hospital teacher-clinical investigators (phase 1 and 2) in designing the most critical studies of the safety and effectiveness of new drugs.

Whether the medical profession as we know it will participate more in the future than has been possible since 1962 in mass clinical trial (phase 3) before new drug approval by governmental authority remains to be seen.

The final approbation or disapproval of a drug after NDA approval (phase 4) will continue to be in the hands of the participating physician as long as he can establish scientifically that the drug is the best possible agent for him to use in healing the sick and comforting the dying.

THE PURPOSE of this presentation is to crystallize the most cogent facts and mention certain of the opinions that have been expressed* with regard to government regulations and the use of drugs.

*Reference Nos. 3, 4, 6, 7, 12, 16, 20, 25.

Presented at a scientific conference, Department of Anesthesia, Stanford Medical Center, 20 May 1966.

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Submitted 18 August 1966.

Reprint requests to: 418 Palm Street, Palo Alto 94301.

Specifically, I want: (a) to clarify the current regulations regarding clinical investigation of a nonintroduced (new) drug; (b) to define more precisely not only the dependence of industry on the scientific community, and particularly the physicians in academic medicine who are qualified to test new drugs in man, but also the obligation of those clinical investigators as well as all physicians in clinical medicine to report all pertinent informa-

tion on new drugs to the governmental officials in the Food and Drug Administration (FDA) of the United States Department of Health, Education and Welfare; and (c) to mention the need for clarification of the role of the qualified physician in clinical medicine in the approbation or disapproval of a new drug before the FDA has sanctioned the chemical compound for marketing.

Government laws effective 1 February 1966, regulating the addictive aspects of drugs (drug abuse control) are not a concern of this synopsis; the emphasis here relates to the changes facing physicians in order to better evaluate new drugs and speed the flow of needed therapeutic tools to their patients.

The 1962 amendments (Public Law 87-781)²³ do not represent an entire revision of the Federal Food, Drug and Cosmetic Act.

Since the passage of the 1938 law, the introduction of a new drug into the United States market has required the approval of the FDA through a new drug application (NDA) approval. Up until 1962, if the FDA did not take action within six months after the application was filed, the manufacturer automatically was allowed to market the drug. Now there is no longer any automatic clearance of new drugs for the market by lapse of time without FDA action, as under the previous law. A new drug cannot be marketed until the FDA approves it as meeting the requirements for safety and effectiveness.

The law recognizes that medical research must go on. Under the 1962 amendments, experimental drugs are exempted from the safety clearance requirements of the law when shipped to qualified investigators for research purposes. However, the testing of new drugs and antibiotics on humans can be prevented under the law unless specified safety conditions are met. In order to meet these safety conditions, the manufacturer must report to the FDA by means of a "Notice of Claimed Investigational Exemption for a New Drug" (IND). This is a form which the regulations have precisely defined (FD1571) in order that all the pertinent facts about the new compound be submitted under ten specific headings. As soon as this is filed, the sponsor or manufacturer can begin research on the drug in man, all research in the United States up to this point having been preclinical and chiefly toxicological to document the safety aspects.

The amendments spell out the direction the planned investigation must follow. Phase 1 starts when the new drug is first introduced into man,

and this is denoted as human pharmacology. Phase 2 covers the initial trials on a limited number of patients for specific disease control or prophylaxis purposes (selected therapeutic trial). Phase 3 is the stage of inquiry bearing on the assessment of the drug's safety and effectiveness. Specifically, the sponsor must establish the range of optimum dosage schedules in the diagnosis, treatment or prophylaxis of *groups* of subjects involving a given disease or condition (mass therapeutic trial). The amendments require that the sponsor report the progress of the investigators to the FDA once yearly. They also stipulate immediate documentation of any serious or life-threatening adverse reactions. At this point, as the pattern of the results of clinical studies takes form, the sponsor assembles the data and presents them to the FDA for NDA. If approved, the compound is marketed.

The amendments require the sponsor or manufacturer to report to the FDA any information on adverse effects or other new clinical experience with new drugs and antibiotics after they are marketed (phase 4). In practice, physicians contact the manufacturer for information. The Medical Department physicians then attempt to develop a complete Drug Reaction Report form with the attending physician's assistance. This form is then transmitted by the manufacturer to the FDA.

Signed agreements from investigators—FD1572 for phase 1 and 2, FD1573 for phase 3—must be obtained by the sponsor and submitted to the FDA, stipulating that the proposed investigations will be under the personal supervision of the investigator signing the form, that the experimental drugs will not be supplied to others and that experimental use on humans is permitted only if the clinical investigator agrees to tell his patients about the experimental status of the drug. Commissioner James L. Goddard recently has spelled out the exceptions to these requirements.⁹

The use of drugs in man is like a tool or an instrument of the physician for the treatment of the sick and protection of the healthy.

The medical doctor participates at every stage in the creation, development, evaluation and use of a drug.⁵ The omnipresence of governmental authority's interest together with that of the university medical school in all aspects of therapeutics is borne out by the history of medical education and medical practice in the United States from colonial times to the present.^{8,22} The first concern shown by governmental authority, about a "receipt [re-

cipe] of curing cancer," was recorded in the 1748 proceedings of the House of Burgesses of the General Assembly of Virginia.¹¹

Four periods might be mentioned, based on the role governmental authority has played in relation to control of the physician's therapeutic tools: 1748-1906, 1906-1938, 1938-1962, 1962-1966. For each period, certain questions can be raised as to what was done and what was left undone at that time.

1748-1906 William Withering was born in 1741 and graduated in Medicine at Edinburgh in 1766. Up until 1906 when the chemist Wiley was the main force behind Congress passing the first food and drug control law, Withering might be considered to be a representative, in an extraordinary manner, of the developer of a new drug of that time. In his experience he embodied an understanding of a clinical need and of the folklore of his community—a "family receipt" [recipe] for cure of dropsy, kept a secret by an old woman in Shropshire. He was an unusual student of botany, having published a treatise on plants in his region of England in 1776, and suspected the active ingredient of the dropsy cure to be foxglove (*Digitalis purpurea*). Finally, he used the approach of the modern clinical investigator as revealed by his monograph,²⁶ with its case histories of *each* patient to whom the drug was given.

In the United States a physician was instrumental in starting the *Pharmacopoeia of the United States* in 1820, the American Medical Association was founded in 1847, and in 1875 the first university hospital (Hospital of the University of Pennsylvania) was established—all key events breaking up the long period of growth in this country of medical education and medical practice. A nihilistic approach to drug usage in the 19th century was described by Osler, one of America's great medical teachers and thinkers.¹⁹ Already in Withering's time apothecaries were on the scene, and they played an unusually prominent role in the use of drugs from colonial times on, into the 20th century.²²

1906-1938 The influence of pharmacists persisted almost up to 1938, when the first food and drug law was completely rewritten in the attempt to provide a more realistic basis of regulation by governmental authority. In this period the relationship between the all-encompassing physician, as Withering was, and the sick person was giving way to the relationship of the patient, physician and

the drug manufacturer who supplied the substance to be compounded by the pharmacist. Between 1905 and 1935 basic new drugs were added to the *U.S. Pharmacopoeia* at an average rate of six per year.¹⁸ From 1905 to 1956, the American Medical Association's Council on Pharmacy and Chemistry, later the Council on Drugs, also passed on drugs before they could be advertised in the Association's publications and listed in its books.⁴

The Federal Pure Food and Drug Act passed in 1906 was basically unchanged until 1938. It prohibited sale in interstate commerce of adulterated or misbranded products. This law was significantly strengthened in 1938 after the tragedy of the distribution, without animal testing, of a sulfa drug elixir in the southeastern United States in 1937. The vehicle, diethylene glycol, proved to be poisonous and was causally related to the death of about one hundred patients before the compound could be removed from the market.

1938-1962 The introduction of sulfa drugs into medical practice in the United States by Perrin Long and Eleanor Bliss at Johns Hopkins Hospital in 1936 might be considered to be the true beginning of the 1938-1962 period. The 1937 tragedy brought government more into control of drugs as far as safety was concerned.

1962-1966 There is still the basic relationship of physician, patient, pharmacist and drug in concert with governmental authority. In the period from 1945 to the present, we have seen an upsurge in "public interest," together with greater dissemination of "product information" to the physician by the profit-motivated pharmaceutical industry.

The most outstanding feature undoubtedly is the amount of sales dollars put into the research and development efforts of the United States drug industry. In 1950, 39 million dollars was spent and the preliminary estimate for 1966 was 355 million. In this period, company financed research and development rose from 4 per cent to nearly 10 per cent of sales.*

Research capabilities of the pharmaceutical industry are divided into three major categories: (a) preclinical, before IND filed, (b) after IND filed, clinical or human pharmacology and selected therapeutic trial, (c) mass clinical trial for NDA and post-NDA marketing surveillance.

*From Chart V, *Key Facts on the U. S. Prescription Drug Industry*, January 1966, distributed by Pharmaceutical Manufacturers Association, Washington, D.C. 20005.

In 1966 the problem of judging whether a new drug application (NDA) is to be approved is more complex than ever before.

In a statement presented by George P. Larrick¹⁷ on 24 March 1964, the then FDA Commissioner explained "How the Food and Drug Administration Evaluates New Drug Applications." Larrick pointed out that, "The average practicing physician, skilled as he may be in making daily decisions with regard to individual drugs to be administered to individual patients, is not necessarily qualified to make the broader decisions about permitting nationwide marketing of a drug."

The FDA must decide now whether the compound is *effective* for the indication as well as safe. Effectiveness is relatively simple to measure in testing an antihypertensive agent in patients. But what about the problem of evaluating quantitatively the effectiveness of a compound proposed to allay the symptoms of the anxious patient—for example, meprobamate? This is controversial.*

Or stated in another way, how probable in the years ahead is the participation of more clinicians in the phase 3 testing of new drugs? That a change from the period of 1962-1966 is needed seems clear. Both James Appel¹ and James Goddard⁹ have stressed the desirability of more qualified physicians taking part in the assessment of new drugs in the gap between pharmacology and therapeutics.¹² The degree of dissatisfaction of clinicians with the complexity of the paper work associated with drug investigation and the precise hindrances needs to be documented now.¹³ The survey published by William Kirby in 1964 was a limited sampling of the reaction of certain physicians in academic medicine and reflected the early 1963 apprehension.¹⁵ Appel's suggestion that the council of the specialty society is the logical arena in which physicians might work toward a change seems realistic.¹

Wolferth set forth his ideas about the possible contribution of clinicians in medical research in 1959.²⁷ At the risk of diminishing the importance of the entire essay, one paragraph out of context is quoted:

"Clinicians occupy a strategic position sometimes overlooked by those who write about how medical research should be done and who should do it. Clinicians are close to the raw material of clinical science. They sit by the bed side, agonize over the patients who look to them for help, and

ask themselves questions that might not occur to the most analytical career investigators. In the past, such questions have constituted an important source of stimulation to clinical science as well as technologic research. One wonders whether Addison and Mackenzie would have done as well as full-time career investigators."

It would seem a tragic loss to American medicine if the 1962 regulations impede or prevent the contributions of future clinical scientists of the Wolferth mold to the clinical assessment of new drugs.

Krantz¹⁶ has expressed the opinion that the part of the 1962 law regarding the establishing of efficacy should be changed. Another opinion is that expressed by the former Medical Director of the FDA, Joseph F. Sadusk, Jr.²¹ He urged that present drug legislation be thoroughly enforced before any new measures are adopted.

"The basic Food, Drug and Cosmetic Act of 1938," Dr. Sadusk said, "together with its several Amendments up to and through 1965, now give the Food and Drug Administration sweeping authority to monitor and control the development, production and use of drugs. It assures us that these drugs will be of high quality and that they will be effective. It provides for the continuing surveillance of drugs so that if there is a significant change in the status of any drug the physician can be informed promptly. But in carrying out the intent of the law there are a number of problems, chief among which is the careful planning and effort which must go into the implementation of that law. Here, the scientific community, the pharmaceutical industry and the Food and Drug Administration itself must develop a degree of expertise which was not dreamed of a decade ago. Organizational structures for such scientific and regulatory purposes are not accomplished in a year or two—the matter is so complex and properly qualified manpower is in such short supply that a half decade or more will be needed to fully implement the law. It would be a mistake to believe that this can be done in less time. Furthermore, the mission cannot be achieved successfully by any one of the group alone. The goal will be reached only as a joint and coordinated effort of the medical community, the industry, and the government. Fortunately, the Congress has amply supported this effort by substantial appropriations of funds but the real bottleneck remains that of manpower."

What, then, in the years ahead, is the prospect for more practicing physicians assisting in the de-

*Reference Nos. 2, 10, 14, 24.

velopment of new drugs in phase 3 before they are approved for marketing by the FDA? From what has been presented, there seems to be an increasing awareness of the potential contribution by the clinician. However, the 1962 law states that clinical investigations should be carried out by "experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved." Change to the extent that more expert clinicians are involved in evaluating new drugs seems obvious. What is also clear is that the final approbation or disapproval of a drug after NDA approval (phase 4) will continue to be in the hands of the practicing physician as long as he can establish scientifically that the drug is the best possible agent for him to use in healing the sick and comforting the dying.

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Recent Advances in Artificial Pacemakers

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■ *Electronic pacing is now the accepted therapy for patients with symptomatic slow ventricular heart rates. Pacing may be temporary or permanent, epicardial or endocardial, fixed, synchronous or demand. The choice of pacing mode is dictated by the clinical status of the patient, his progress during temporary pacing, and the presence or absence of competitive rhythm.*

THE INTRODUCTION OF implantable electronic cardiac pacemakers by Zoll,¹⁸ Chardack,⁷ Parsonnet,¹⁴ Furman⁹ and others has resulted in a profound change in the treatment of patients with heart block. It has now been amply demonstrated that artificial pacing is a reliable procedure and is the treatment of choice in patients with symptomatic slow heart rates. It is the intent of this paper to review the subject of pacemakers, stressing particularly the basic units currently available and the indications for each type. Some comments will be made about unusual types of pacemakers and prospects for the future.

Basic Pacemaker Characteristics

Pacemakers, both internal and external, have quite similar output characteristics consisting of uniphasic or biphasic pulse waves of from 1.5 to 2.0 milliseconds duration, energy outputs from 65 to 200 microjoules, and peak currents in the range of 7.5 to 14 milliamperes.¹³ This provides sufficient energy to pace the heart in the majority of patients by epicardial or endocardial electrodes

and will also accommodate the rising pacing threshold which may develop over a period of two to three months following implantation. Pulse generators consist of electronic components and mercury cell batteries imbedded in inert epoxy resins. They are connected to the stimulating electrodes by means of coiled wire leads covered with a protective layer of silicone rubber.⁴

Pacemaker Types and Clinical Applications

Pacemakers currently available may be classified by their particular functional characteristics such as lead design (epicardial or endocardial), mode of pacing (fixed rate, synchronized, demand), duration of pacing (temporary or permanent) and power supply (battery, radiofrequency induction, magnetic field induction, mechanical-energized, chemical-energized or atomic power). Some of the characteristics of commonly used pacemakers are grouped and summarized in Table 1 and Figure 1.

The selection of the desired pacing mode is guided by two principles, one clinical, the other electrocardiographic. Clinically, the presence of complications (such as diabetes, renal disease and congestive failure) favors the safer endocardial approach.⁸ Electrocardiographically, the presence of competitive foci (patient and pacemaker) may make either synchronous or demand pacing the method of choice.^{1,15} Table 2 outlines our prin-

This work was supported in part by USPHS Grant HE 09298-02, and the Los Angeles County Heart Association, Research Award No. 382.

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TABLE 1. — *The Basic Types of Pacemakers in General Use Today*

| <i>Duration of Pacing</i> | <i>Pacemaker Electrode Location</i> | <i>Pacing Mode*</i> |
|---------------------------|-------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------|
| Temporary..... | Endocardial..... | 1. Continuous stimulation with manually variable rate and voltage 2. "Demand" stimulation with manually variable controls for rate and voltage |
| Permanent..... | Endocardial..... | 1. Fixed rate and voltage 2. "Demand" with fixed controls for rate and voltage |
| | Epicardial..... | 1. Fixed rate and voltage 2. "Demand" with fixed controls for rate and voltage 3. P-wave synchronized with fixed voltage |

*All commonly available pacemakers, both internal and external, have a fixed pulse duration set by the manufacturer.

ciples for pacemaker selection. Rapid advances in electronic circuitry may well modify present guidelines.

Temporary Pacemakers

Initial control of slow heart rates is obtained by the use of a temporary right ventricular pacing catheter.⁷ Temporary pacing affords the following

benefits: Improved myocardial reserve and relief of congestive heart failure; cessation of Stokes, Adams attacks; an opportunity to analyze, control and treat azotemia, anemia, infection, electrolyte and pH disturbances; maintenance of adequate heart rates while using bradykinetic drugs (digitalis and quinidine); and control of heart rates during the elective implantation of a perma-

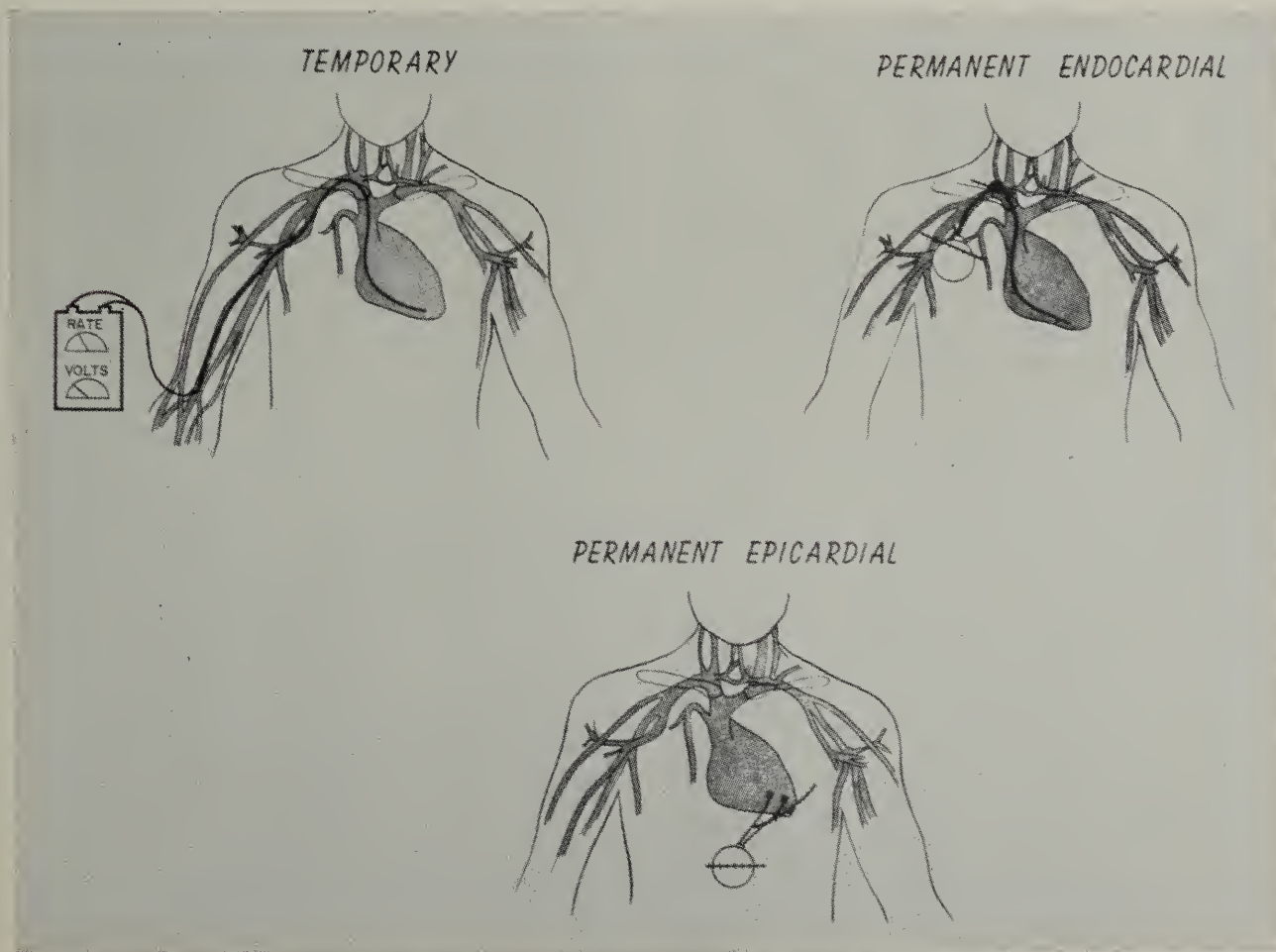


Figure 1.—Pacemaker implantation may be temporary, permanent endocardial via the right external jugular vein or permanent epicardial through left thoracotomy.

TABLE 2.—Criteria for Pacemaker Selection

| Group | Diagnosis | Symptoms and Complications | Rhythm | Temporary Pacing | Type of Permanent Pacemaker |
|-----------|------------------------------------|--------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|------------------------------------------|------------------------------------------------------------------------------------------------------------|
| I..... | Acute myocardial infarction | None Adams-Stokes Congestive heart failure Shock | Second or third degree block Sinus arrest, intermittent or sustained | Ventricular demand | Only with sustained (more than 1 mo.) block. Then place in Groups II. |
| II..... | Chronic heart block | None | Second or third degree block with basic rate above 30/min. | None | Place in Group II A-D if any symptoms. |
| II A..... | Chronic heart block | Adams-Stokes Congestive heart failure Cerebral or coronary insufficiency | Second or third degree block Sinus arrest Rate less than 30/min. | Either ventricular demand or fixed rate* | Dependent upon patients' rhythm and clinical status according to the following criteria. |
| II B..... | Chronic heart block | Adams-Stokes Congestive heart failure Cerebral or coronary insufficiency | Second or third degree block with normal sinus activity Rate less than 30/min. | Either ventricular demand or fixed rate* | <i>Epicardial</i> : P-wave synchronous or ventricular demand. <i>Endocardial</i> : Ventricular demand. |
| II C..... | Chronic heart block | Adams-Stokes Congestive heart failure Cerebral or coronary insufficiency | Second or third degree block Inadequate sinus activity† | Either ventricular demand or fixed rate* | <i>Endocardial</i> : Fixed rate* or preferably ventricular demand. |
| II D..... | Chronic heart block | Adams-Stokes Congestive heart failure Cerebral insufficiency | Intermittent A-V block with any type of supraventricular rhythm | Ventricular Demand | <i>Epicardial</i> : Either P-synchronized or ventricular demand <i>Endocardial</i> : Ventricular demand |
| III..... | Sinus arrest | Adams-Stokes Cerebral or coronary insufficiency | Intermittent sinus arrest | Ventricular Demand | <i>Epicardial</i> : Ventricular demand <i>Endocardial</i> : Ventricular demand |
| IV..... | Malfunctioning permanent pacemaker | With or without symptoms | | Ventricular Demand or fixed rate* | Repair or replace |

*If a fixed rate pacemaker is used its rate should be sufficient to inhibit competitive rhythm.

†Atrial fibrillation, atrial flutter, sinus arrest, low atrial potential.

nent pacer. The normal heart rate afforded by temporary pacing changes stroke volume and heart size. Heart size is of vital importance when related to permanent endocardial catheter positioning, fixation and possible perforation. Temporary pacing allows adequate time for a clinical and electrocardiographic appraisal, leading to an optimal choice of a permanent pacer and lead system.

Acute Myocardial Infarction

A-V block and sinus arrest are grave complications of acute myocardial infarction.¹⁰ Evidence is accumulating that the development of second and third degree A-V block, even when entirely asymptomatic, is a specific indication for insertion of a right ventricular pacing electrode.¹⁶ Our present recommendation is that a temporary catheter with a demand pacemaker be used³ in any patient with acute myocardial infarction who has second or third degree heart block or periods of sinus arrest. This form of therapy is simpler, more effective, and probably safer than the pharmacologic approach which is the alternative means whereby ventricular rate may be augmented. The positive inotropic effect of drugs such as isoproterenol may be desirable in patients with myocardial infarction. However, the chronotropic response can be quite hazardous, with occasional production of ventricular tachycardia or fibrillation. The pacing catheter with demand features should be left in place for a period of two weeks after the return of normal sinus activity.

Permanent Pacing—Endocardial versus Epicardial

Epicardial pacing of the heart requires the suturing of electrodes to the left ventricular epicardial surface. Since the average age of patients who require artificial pacemakers is approximately 75, the increased mortality and morbidity from thoracotomy becomes an important consideration. This is particularly true in the presence of diabetes, renal or cerebrovascular disease.⁸ For this reason, extrapleural approaches have been employed, including:

1. A parasternal extrapleural incision to avoid entry into the left chest. Only limited visualization of the myocardium is possible and a sensing electrode cannot be sutured to the atrium for the purpose of synchronized pacing.
2. A subdiaphragmatic approach through an epigastric incision. Again, atrial electrode attachment is not possible.
3. Placing of endocardial pacing electrodes through a peripheral vein. This alternative to

standard thoracotomy is the most promising and many observers consider it the implantation procedure of choice. By the use of this technique, morbidity and mortality are decreased. Ease of installation and simplicity of replacement of the pulse generator and lead system are important additional advantages. The feared complication of thromboembolism has not materialized and anticoagulants are unnecessary since an endothelial envelope forms very rapidly over the catheter.¹² The disadvantages are relatively few. Approximately 10 per cent of patients with endocardial pacemakers have displacement of the pacing catheter tip from the right ventricular apex.¹¹ As a general rule this follows faulty initial placement and is thus a technical problem. Recently catheters with flared tips have facilitated permanent implantation. There is no successful and simple method of synchronized pacing using endocardial electrodes, although Carlens and coworkers⁵ recently described a technique for placing an atrial pick-up electrode above the right atrium by mediastinoscopy. Bacterial endocarditis may be a hazard in patients with valvular heart disease and endocardial pacing.

Competitive Rhythm

Twenty-five per cent of patients who are permanently paced for third degree block return to normal A-V conduction.¹⁷ When this occurs, a "competitive" state is established between depolarization of the ventricles produced by the artificial pacemaker and that produced by the patient's own sinus pacemaker (Figure 2). Following the restoration of normal A-V conduction, it is inevi-

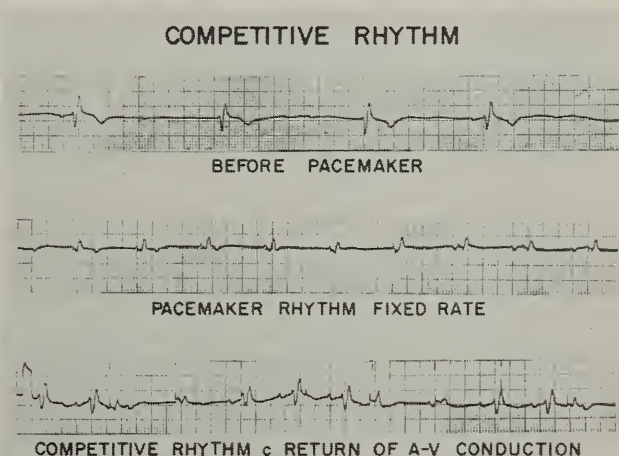


Figure 2.—Competitive rhythm. If, following the implantation of a permanent pacemaker, normal atrio-ventricular conduction should return, "competition" will take place between the patient's sinus rhythm and the pacemaker.

table that an electrical stimulus from a fixed-rate pacemaker will discharge during the vulnerable period of the cardiac cycle. We have shown that when the vulnerable period is occupied by a pace-making stimulus, rapid repetitive beating or ventricular fibrillation may occur.¹ Indirect support for this observation has been obtained by Sowton,¹⁷ who found a five-fold greater mortality rate in patients who returned to sinus rhythm than in persons remaining in third degree block. When competition occurs in the presence of myocardial anoxia, acidosis, electrolyte imbalance or myocardial infarction, ventricular tachycardia and fibrillation are even more likely to occur.

It should be stressed that competitive rhythm may be a mortality factor in either temporary or permanent pacing. In fact, during temporary pacing, patients are more likely to have associated problems which predispose to the formation of

ectopic rhythm. Mounting concern over competitive rhythm has stimulated the development of ventricular demand pacemakers (for both temporary and permanent pacing) and a renewed interest in synchronized permanent pacemakers.

P-Wave Synchronized Pacemakers

If a patient's own atrial potential is used to "trigger" the ventricle, competition may be prevented (Figure 3). A sensing electrode is attached to the atrium and the electrical signal produced by atrial depolarization is transmitted to the pacemaker.⁶ A delay (equivalent to a P-R interval) is then followed by stimulation of the ventricle by means of electrodes attached to the epicardial surface. Thus with each effective atrial depolarization there will follow, at a fixed predetermined interval, activation of the ventricles by the artificial pacemaker. Safeguards are, of course, necessary with

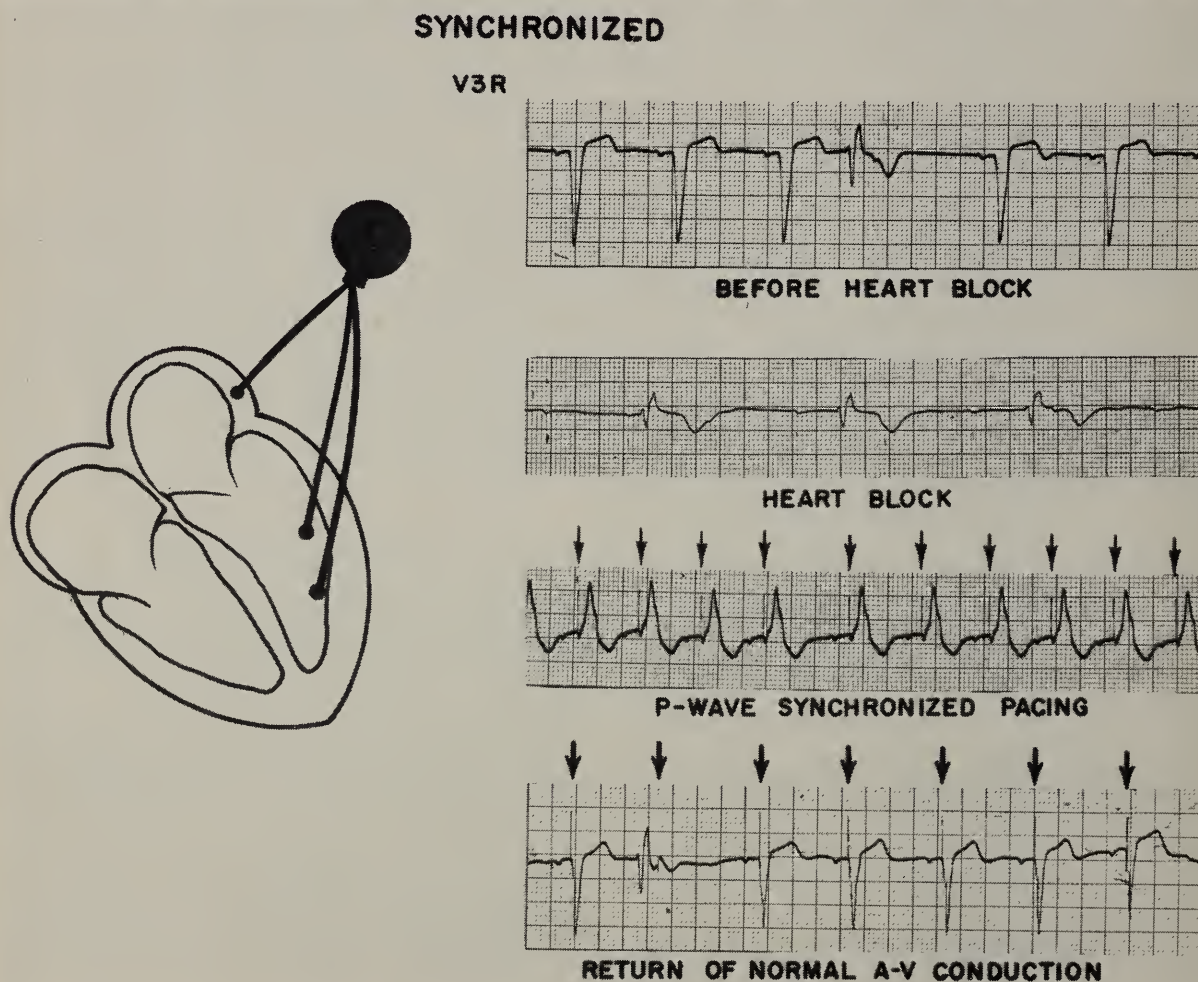


Figure 3.—Synchronized pacemaker. If, following the implantation of a synchronized pacemaker, normal atrio-ventricular conduction should return, "competitive" rhythm will not occur. Arrows indicate artificial pacemaker impulses. V3R=Third ventricular lead, right side.

this type of pacemaker. If no signal is received from the atrium (due to a break in the atrial wire or ineffective atrial depolarization or an electronic failure) the pacemaker will revert to a fixed rate. If the patient's rate becomes too rapid (atrial tachycardia or atrial flutter) electronic blocking is induced to maintain a physiologic rate. Most synchronized pacemakers are designed to work in a range of approximately 60 to 120 beats per minute. Principal disadvantages to synchronizing pacing are the necessity for thoracotomy, the complexity of electrical circuits required and the need for more frequent battery replacement.

Demand Pacemakers

The use of a pacemaker designed to operate only when there is an inadequate ventricular rate (Figure 4) is quite appealing and is the second way in which competitive rhythm may be prevented.¹⁵ An electrode is used for the dual purpose of detecting ventricular systole and stimulating the ventricle. A sensing unit is incorporated which will detect an R wave above a minimal predetermined magnitude (usually 2 to 4 millivolts). Electronic filters inhibit P and T waves and exter-

nal electrical sources. When the patient's R-R interval is longer than that which is usually considered safe, the pacemaker is activated and the heart is paced at a fixed rate. Any subsequent R-R interval (including the pacemaker-induced beats) equivalent to a safe rate results in pacemaker shutdown and the cessation of artificial stimulation. The difference between the rate required to turn the pacemaker on and that which will turn it off is deliberately regulated so that stimulation will occur only during the QRS portion of the electrocardiographic cycle.

Such a pacemaker presents distinct advantages. Competition between the patient's intrinsic focus or foci and the pacing unit is prevented. Artificial stimuli will fall only during the QRS portion of the cardiac cycle, and during this time the ventricles are completely refractory. The presence of a rate above the demand threshold, as well as simplified circuitry, will conserve battery life. Rapid heart rates do not require electronic control as is now necessary with P wave synchronized pacemakers, and premature ventricular contractions effectively block the pacing unit.

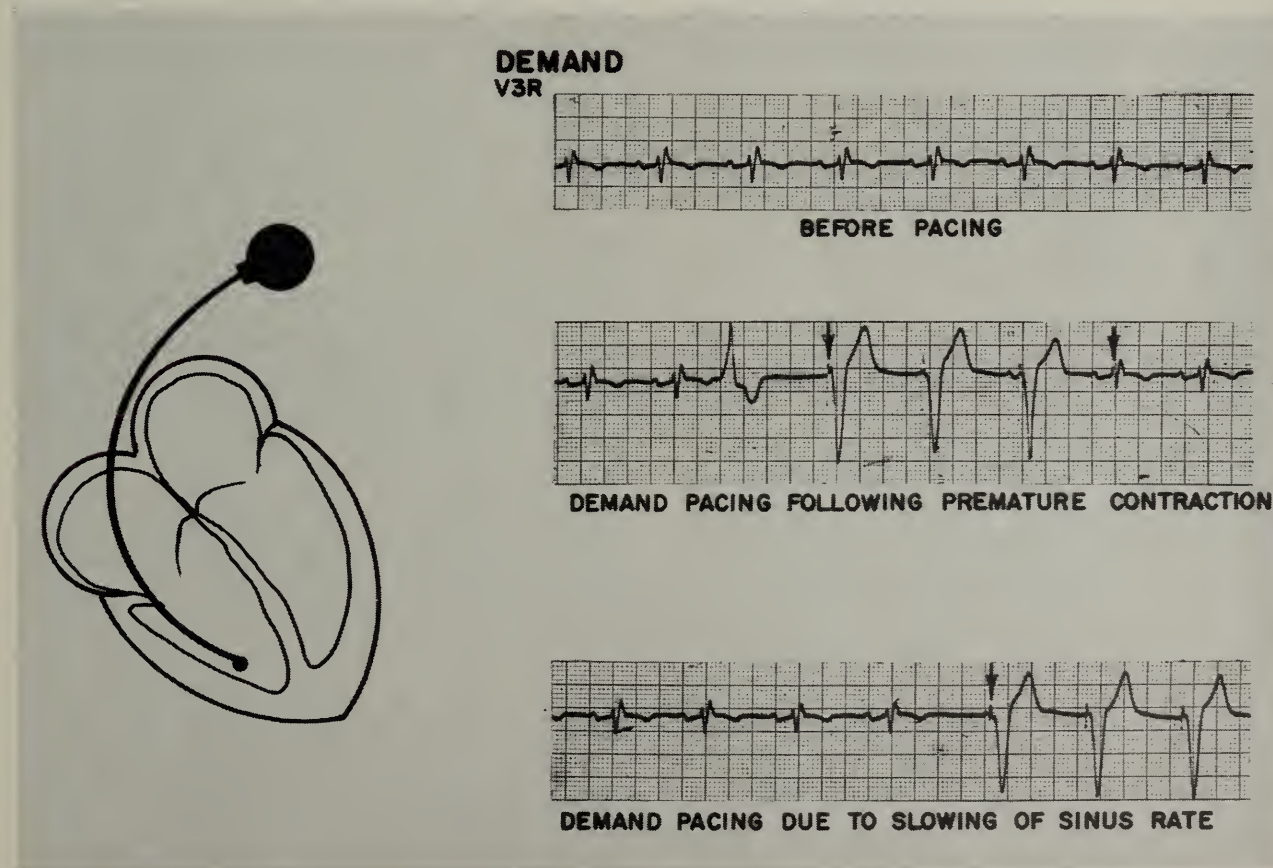


Figure 4.—Demand pacemaker. If, following the implantation of a demand pacemaker, the patient's R-R interval is at a satisfactory rate the pacemaker will not function. If, on the other hand, the R-R interval becomes too long, the pacemaker automatically turns on. Arrows indicate beginning and end of pacemaker stimulation. V3R=Third ventricular lead, right side.

A number of unique problems arise with demand pacemakers. External electrical sources can usually be adequately screened. We have shown, however, that as little as 1 volt from an external pacemaker will control the internal demand of one commercially available unit.² Certain radio-frequencies may interfere with demand pacemaker function by a similar mechanism. To prevent pacemaker shut-down from external sources, "standby" pacemakers have been designed. The standby pacemaker discharge is synchronized with the patient's own pacemaker focus as long as the heart rate is above 70 per minute. An artificial electric pacer stimulus is programmed 20 milliseconds after the patient's own QRS, thus avoiding the vulnerable period. However, when the rate is less than 60 per minute, synchronization is lost and demand pacing takes place. With this circuitry, high frequency external electrical sources are less likely to interfere with the demand function of the pacemaker.

A simple method must be found for a routine check of demand function. Bradycardia produced by carotid sinus stimulation may be used as a check upon pacemaker function when A-V conduction is intact. However, inconsistent response to vagal stimulation and the risk of producing asystole in the presence of a defective pacemaker make this procedure hazardous.

Future Pacemaker Design

Refinements in electronic circuitry and lead design have improved pacemaker performance. Little progress has been made, however, in the development of long term energy sources.¹² Biologic and atomic sources of energy are experimental and have not had sufficient clinical trial. Although rapid advances are being made in circuitry, in power supply and in lead systems, it is imperative that simplicity be maintained with any future alteration in pacemaker design in order to have a continued high degree of pacemaker reliability.

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CASE REPORTS

Osteogenesis Imperfecta and Pregnancy

Report of a Case in California with
Notes on Management

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OSTEOGENESIS IMPERFECTA is a rare disease of unknown cause with a slightly greater incidence in females than males. It probably involves a congenital defect of collagen, with defective collagen in bone, sclera, ligament, skin and other tissues.

The main feature of osteogenesis imperfecta is abnormal bone development with thin and poorly formed cortices, diminished osteoplastic and osteoclastic activity and poor periosteal and endosteal deposition.⁹ Susceptibility to fractures is greatly increased. The severity and prognosis of this disease are widely variable, but are closely correlated with the age of the patient at the time of the first fracture. The tendency to fractures regresses at the time of puberty and skeletal maturity, but in women it may increase again after the menopause.⁸

Osteogenesis imperfecta commonly involves a triad of findings. In addition to frequent fractures (50 to 75 per cent of cases), blueness of sclerae is noted in 90 to 100 per cent and conductive type deafness in 25 per cent. Excessive translucency of the sclerae allows the choroid to show through it. Other findings sometimes associated with osteogenesis imperfecta include thinness of skin, hypermobility of joints, and facies of triangular shape with bitemporal protuberance and prominent frontal bone.^{8,2}

Nomenclature of this disease embraces a con-

fusing array of terms, but the essential types are osteogenesis imperfecta congenita, which begins in utero and usually causes death before birth or in the first year of life, and osteogenesis imperfecta tarda, the more common form, which usually becomes manifest in childhood, often in the second decade of life. The incidence of osteogenesis imperfecta congenita has been reported by various investigators as ranging from one case in every 20,000 to 60,000 deliveries, but the incidence of osteogenesis imperfecta tarda is certainly higher.^{2,7}

At present, there is no histological or chemical procedure to establish the diagnosis. Osteoporosis is visible roentgenographically.⁴ Serum calcium and alkaline phosphatase are normal. Fertility and pregnancy per se are unaffected by osteogenesis imperfecta.¹ There is no specific treatment for this disease. Corticosteroids have generally not helped, nor have parathormone or anterior pituitary extracts.³

The purpose of this report is to present a case of osteogenesis imperfecta in pregnancy and a review of considerations for management of prenatal course and delivery.

Report of a Case

A 19-year-old primigravida was first seen in December 1965 with history of last menstrual period 14 June 1965. She had been found to have osteogenesis imperfecta at two years of age when a fracture occurred. She later had a total of 17 fractures, mainly in the long bones, the most recent one when she was 15 years old. Numerous orthopedic procedures had been necessary between ages 6 and 15, and the patient had intramedullary rods in both femurs and both tibias. Her menstrual history was quite normal. An audiogram made at age 16 was within normal limits. The patient's family history did not reveal any instances of recurrent fractures, blue sclerae or other stigmata of osteogenesis imperfecta. She had three sisters in good health. The patient had been essentially asymptotic

Submitted 30 March 1967.

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matic since age 15, and did not complain of bone pain.

Physical examination revealed a normal intrauterine pregnancy at about five and one-half months gestation. The sclerae were blue and the forehead showed frontal bone prominence. The patient's development otherwise appeared normal, and she walked easily without limp or deformity. Range of motion of all joints was normal. Pelvic examination showed clinically adequate pelvic dimensions. Routine laboratory studies were within normal limits except for hematocrit of 34 per cent.

The patient was treated with iron by mouth and was observed through an uneventful prenatal course. Weight gain was 16 pounds. Results of x-ray pelvimetry in February 1966 were within normal limits and there were no apparent fetal abnormalities. The patient's bones were noted to be osteoporotic. In March 1966 a scout film revealed no fetal fractures. After spontaneous nine-hour labor at term, a normal vaginal delivery of a seven pound ten and three-fourths ounce girl was carried out. A right mediolateral episiotomy and pudendal block anesthesia were used. The patient tolerated the dorsal lithotomy position during delivery without difficulty. There was no excess bleeding or any other postpartum complications. X-ray examination of the pelvis after delivery showed no fractures.

The infant had an Apgar score of 9 and showed no abnormalities on physical examination except for slightly bluish sclerae. There was no evidence of any fractures or deformities, and muscle tone was normal. She was followed until seven months of age, and development was normal to that time in all respects.

Discussion

Management of pregnancy and labor in patients with osteogenesis imperfecta is very similar to that of a normal situation.¹ There is no special indication for interruption of pregnancy in a patient with this disease. There seems to be a somewhat greater need for administration of iron by mouth in the prenatal period. X-ray films should be taken late in pregnancy to evaluate pelvic dimensions and possible fetal fractures. To reduce the risk of fractures, special care should be taken in positioning the patient for delivery, and x-ray films of the maternal pelvis should be made in the postpartum period. Indications for vaginal delivery or cesarian section are the same as in any other pregnancy. Osteogenesis imperfecta congenita can be easily

recognized at birth by deformity of extremities or softness and pliability of the cranium, and often the infant is stillborn.^{2,5}

The genetic basis for this disease is not firmly established. In one series of 16 infants with osteogenesis imperfecta congenita, 12 had no family history of the disease.² A postulation of dominant genetic transmission is favored, but genetic "penetrance" is often so slight that descendants are not affected; unaffected children of an affected parent are not thought to transmit the disease.⁸ Sporadic cases are probably mutative.⁶

Summary

A case of pregnancy in a primigravida with osteogenesis imperfecta is presented, together with a discussion of the disease and its management from an obstetrical point of view.

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Atypical Bilateral Temporal Artery Disease

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Diagnosis of temporal giant cell arteritis in patients less than 48 years of age is uncommon,⁴ but examination of sections in random post mortem

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Submitted 15 November 1966.

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examinations showed it to be more common than suspected.¹ It may be an occult lesion,⁷ or the typical histologic phenomena may occur in a vessel other than the temporal artery.⁶ In the case here reported, a 38 year old man had a classical history of the disease but the histopathological findings were unusual. Biopsy of a specimen taken from the left temporal artery showed arteritis without necrosis or giant cells. Eight months later a specimen from the opposite temporal artery showed a dissecting aneurysm.

Report of a Case

A 38-year-old caucasian man was admitted for evaluation to Highland General Hospital. He had first been seen in the Emergency Room in April 1965 with first and second degree burns over the face and hands from a gasoline fire. He was treated with nitrofurazone (Furacin®) dressings and in a month recovered.

At a follow-up visit to the outpatient clinic in May 1965, he first complained of headaches which had begun several weeks before the burn. This pain was located in a 6 cm diameter area in the left temporal region, with radiation to the left temporomandibular joint and anteriorly over the left side of the forehead. The pain was severe, throbbing and lancinating in character, occurred two to three times daily, lasted 15 to 30 minutes, and was relieved by taking aspirin. There was no history of aura, nausea, vomiting, lacrimation, rhinorrhea or allergic disease. In January 1965, however, the patient had noticed episodic facial flushing which, on questioning, he recalled might have been simultaneous with headaches. Administration of aspirin with codeine 30 mg as needed for pain and of phenobarbital 15.0 mg four times a day was begun.

The medical history elicited congenital external strabismus with associated paretic nystagmus. There was no history of familial disease. The patient smoked one to two packages of cigarettes daily and consumed ethanol in small amounts.

In August 1965 the severity of the pain increased and the temporal area became sore. The left temporal artery was swollen and tender. A biopsy specimen was taken. It showed arteritis without necrosis or giant cells (Figure 1.)

After biopsy, prednisone was given, 30 mg daily. Headaches temporarily diminished after the excisional biopsy, but then recurred, and meprobamate, 1.2 gm daily, was added to the regimen.

There was a slow remission over the subsequent months.

In February 1966 mild acne vulgaris developed which was treated with improved skin hygiene and baths with a hexachlorophene emulsion. The patient also said that facial flushing had become virtually constant but still fluctuated somewhat with severity of head pain.

In March he first complained of right temporal headaches associated with tenderness over the temporal artery. These headaches were similar to those on the left side and a specimen was excised from the right temporal artery for biopsy. Headaches persisted without remission after operation and the previously prescribed drugs were continued—prednisone 30 mg daily, meprobamate 1.2 gm daily, aspirin with codeine 30 mg as needed, and antacids.

The patient was again admitted to hospital and on physical examination pronounced erythema of the face and neck was noted and there was decided venous telangiectasis of the forehead and nose, acne vulgaris of the face, back and chest, and external strabismus with horizontal nystagmus on the right. The head was normal in shape and size. In the temporal regions there were two well-healed biopsy sites. Over the remaining right temporal artery there was a slightly tender area 2 cm in diameter. The retinal arterioles were slightly narrowed. Peripheral pulses were normal. There were no subcutaneous nodules or splinter hemorrhages and no enlargement of lymph nodes. Blood pressure on repeated readings averaged 110/80 mm of mercury. On a few occasions the diastolic pressure was 100 mm.

Packed cell volume was 44 per cent and leu-

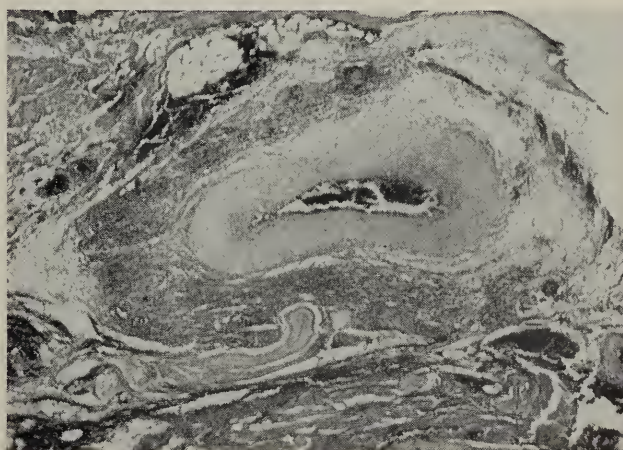


Figure 1.—Section of left temporal artery with perivascular inflammatory exudate. Media is intact. (Hematoxylin and eosin stain, $\times 40$.)

kocytes numbered 13,600 cu mm with segmented neutrophils 64 per cent, band forms 4 per cent, lymphocytes 31 per cent, and eosinophils 1 per cent. The erythrocyte sedimentation rate (Westgren) was 9 mm in one hour. Two L.E. cell preparations were negative. The platelet count was 256,000 per cu mm. A Venereal Disease Research Laboratory (VDRL) test was non-reactive. Results of urinalysis were within normal limits. Blood urea nitrogen was 13 mg per 100 ml. Serum albumin was 4.32 gm and globulin was 1.83 gm per 100 ml. A liver profile was entirely within normal limits. Catecholamines in a 24-hour specimen of urine were 30 mcg (normal under 180 mcg) and 5-hydroxyindolacetic acid was 9.7 mg (normal 0.5 to 7.0 mg). X-ray films of the chest and skull and an electrocardiogram were all within normal limits. Biopsy of the skin and the gastrocnemius muscle biopsy showed no pathologic changes.

In the hospital the patient had episodes of severe right temporal headaches with radiation over the right side of the forehead. These occurred three to six times daily, lasting 15 to 60 minutes and were poorly relieved with analgesics. An attempt to decrease the dose of prednisone was initiated and the patient was discharged to clinic care.

Pathologist's Report

The specimen from the left temporal artery was 0.4 cm in diameter with a small lumen. The wall appeared uniformly thickened but elastic. The right temporal artery was 0.5 cm in diameter. On section the wall was dark red. The lumen was not seen.

On microscopic examination there appeared to be no thrombotic occlusion of the lumen of the left

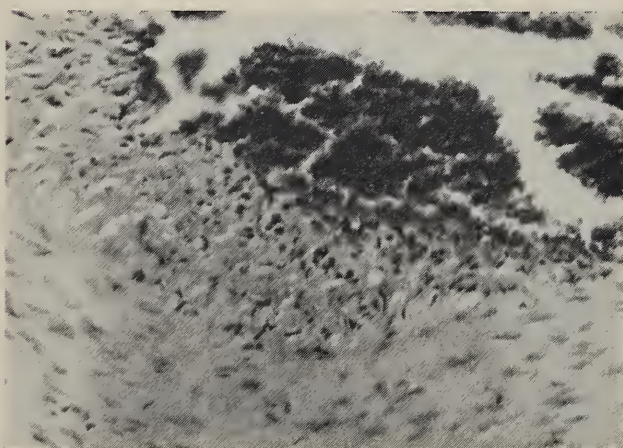


Figure 2.—Subintimal thickening of left temporal artery with few inflammatory cells. (Hematoxylin and eosin stain, $\times 250$.)

temporal artery (Figure 2). A slight focal subintimal thickening of the wall was noted. The elastica and media were intact. In adventitia and surrounding connective tissue there was dense lymphocytic inflammatory infiltration with many scattered eosinophils. No giant cells were seen. A few scattered eosinophils and lymphocytes were present in the subintimal thickening.

In the right temporal artery (Figure 3) a dissecting channel of blood penetrated through the intima and media. The aneurysmal sac was limited by a thin layer of adventitia. The periadventitial connective tissue contained lymphocytes and few polymorphonuclear leukocytes. This inflammatory reaction was less than was seen around the left temporal artery. The intima and media of the dissected vessel showed no inflammation or fibrinoid degeneration. Alcian blue and periodic acid-Schiff staining revealed no acid mucopolysaccharide.

Discussion

That the histologic picture of temporal artery disease is a classic one is emphasized in several of the reviews.^{8,11} The accepted features of it, observed in the first biopsy in the case here presented, are (a) intimal proliferation and (b) inflammatory cellular infiltration of the adventitia and periadventitia (Figure 1). Two histologic features usually described in this disease, but not present in this biopsy specimen, are (a) degeneration of the inner elastica layer with giant cell formation and degeneration of the media of the vessel, and (b) narrowing of the lumen with thrombotic occlusion. Also atypical in the present case were laboratory studies which did not show the usual abnormalities observed in other cases.^{8,11} The patient received prolonged glucocorticoid maintenance therapy (prednisone 30 mg daily from August 1965 through March 1966). Despite this large dose, symptoms referable to the opposite temporal region developed, leading to the excisional biopsy which showed a dissecting aneurysm. (Figure 3) The physical examination of the patient did not suggest any of the features associated with atypical Marfan's disease. Dissecting aneurysm of arteries other than the aorta was reviewed by Watson⁹ and in none of the reports of 23 cases that he cited was a temporal artery involved. In the present case the dissecting episode could not be connected with history of trauma. The special histological stains (alcian blue and periodic acid-

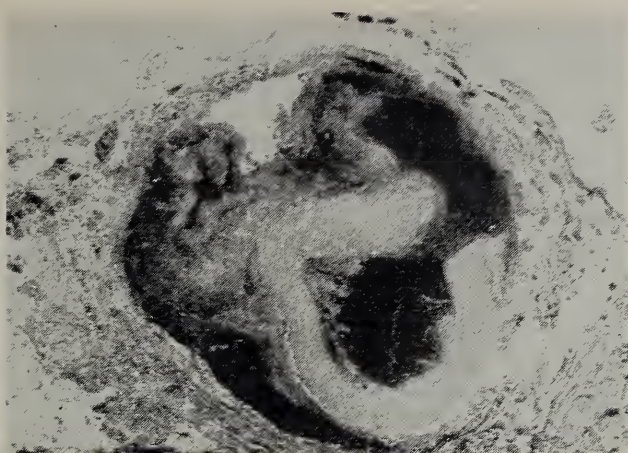


Figure 3.—Dissecting aneurysm of right temporal artery. Perianeurysmal adventitia shows some inflammatory reaction. (Hematoxylin and eosin stain, $\times 40$.)

Schiff) showed no accumulation of mucoid-like material in the wall of the vessel such as is observed in idiopathic necrosis. Watson's classic definition of dissecting aneurysm is pertinent: "The lesion results from penetration of the blood into the wall of the artery, causing a concentric split along the natural lines of cleavage between coats or between medial laminae, extending over a variable distance and usually, but not necessarily, associated with a tear of the inner coat of the vessel."

The concomitant occurrence of dissection with long continued steroid therapy in the present case is interesting because of the reports of dissecting coronary artery aneurysms^{5,10} in which the authors speculated upon the possibility of transitory lathyrism brought about by the changed hormonal status during pregnancy. It may be that in the case herein reported the large maintenance dose of prednisone suppressed the inflammation, since the cellular response to the arterial dissection was minimal (Figure 3) but the intra-arterial collagen tissue was altered ("loosened"⁵) sufficiently to facilitate dissection.

The cause of temporal arteritis is unknown. Its relationship to the autoimmune diseases is uncertain but there is a tendency to include temporal arteritis in the complex scheme of these disorders.² Giant cell aortitis³ and temporal arteritis are considered related but knowledge of the basis of the relationship is sketchy.

The purpose of this communication is to add to the list of variables of temporal arteritis, hoping that widening the scope will, paradoxically, sharpen definitions.

Summary

Unusual manifestations in a case of bilateral temporal artery disease were onset at an earlier than usual age, incomplete histologic manifestations of temporal arteritis in the first biopsy site and recurrence in the opposite side with a histologic finding of dissecting aneurysm while the patient was receiving large amounts of glucocorticoid for maintenance therapy.

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Primary Malignant Mesothelioma of the Pericardium

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PRIMARY PERICARDIAL mesothelioma is rare. Only 29 cases had been reported to 1960,⁷ with an additional eight cases through 1965. In virtually all of them diagnosis was made after death.*

So far as we could determine, the case described below is the first in which the diagnosis was established before death.

*Reference Nos. 2, 6, 11, 12, 15, 16, 20, 22.

Submitted 27 December 1966.

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Report of a Case

A 28-year-old white man, an electrical engineer, first entered the hospital on 7 July 1962 with chief complaint of epigastric discomfort with anorexia of two weeks' duration. He described epigastric pressure radiating to the neck. He admitted to exertional dyspnea but denied cough, fever or chest pain. Aside from these symptoms and excessive fatigue for three weeks, he said he had been in good health.

The patient had never smoked or used alcohol, nor had he any noxious occupational exposures. He had had poliomyelitis with apparent bulbar involvement in 1947. Both parents were living and well.

On physical examination it was noted neck veins were distended while the patient was sitting, without positive venous pulsation. Jugular hepatic reflex was present. Neither the thyroid nor the cervical nodes were enlarged. The anterior-posterior diameter of the chest was moderately increased. Dorsal kyphosis was present. The lungs were clear to percussion. Moist rales were heard over the right middle field and base. The diaphragm appeared moderately elevated with limited excursion.

The heart seemed enlarged, dullness on percussion extending nearly to the left anterior axillary line. The sounds were distant with no audible murmurs. There was a sinus arrhythmia and a small apical friction rub. There was a paradoxical pulse. Blood pressure was 110/70 mm of mercury and the pulse was slightly irregular at a rate of 104.

The liver extended 8 cm below the right costal margin. The spleen was not palpable.

Leukocytes numbered 10,900 per cu mm with the cell differential within normal range. Hemoglobin was 12.9 gm per 100 ml and the hematocrit was 42 per cent. Bilirubin content was 0.95 mg per 100 ml of blood and the serum glutamic oxaloacetic transaminase (SGOT) 20.0 units. Alkaline phosphatase was 3.0 Bodansky units. Results of urinalysis were within normal limits. A test for urobilinogen was positive at 1:20. Cephalin flocculation was negative—2 plus at 48 hours. The sedimentation rate (Westergren) was 12.0 mm in one hour.

No organisms grew on a culture of pericardial fluid and a smear for acid-fast bacilli was negative. The reaction for C-reactive protein was plus 4. A test for lupus erythematosus was negative and there was no clumping of cold agglutinins. Protein

electrophoresis showed total serum protein of 5.7 gm per 100 ml with an albumin:globulin ratio of 3.46:2.24 and α_1 fraction of 2.3, α_2 0.5, β 0.56 and γ 0.87 gm per 100 ml. A Venereal Disease Research Laboratory test was non-reactive.

Subsequent blood cell counts were within normal limits. X-ray films of the chest showed an enlargement of the cardiac configuration with beginning pleural effusion at the left base. Repeated films after pericardial centesis showed a remarkable reduction in the size of the cardiac silhouette and also disappearance of the previously reported pleural effusion. Severe kyphosis of the dorsal spine, slight scoliosis and possibly old compression fractures were noted. An electrocardiogram showed a low voltage pattern and changes suggestive of beginning pericarditis in the sinus tachycardia. Later electrocardiograms show S-T wave changes suggestive of epicardial injury, possibly from pericarditis. On pericardicentesis seven weeks after the patient entered the hospital, 350 ml of bloody fluid was withdrawn and a cell block section showed erythrocytes and clusters of mesothelial cells (Figure 1).

A week later the pericardial cavity was surgically opened. The pericardium was thickened and gray and within the cavity there were dense, gray, fibrin-covered tumors attached to the epicardium. On examination of sections, the tumors were reported as malignant mesothelioma.

The patient was transferred to UCLA Medical Center for chemotherapy. Upon his return home he had transient improvement but his condition then deteriorated rapidly. There were three subsequent brief hospital admissions for adjunctive control of progressing right heart failure, which responded in diminishing fashion to digitalis and diuretics.

Three weeks before the patient died, 27 March 1963, proptosis of the right eye developed and the pupil became fixed. The patient was mentally confused. The entire duration of illness was nine months.

The autopsy findings were: (1) Primary malignant pericardial mesothelioma with direct extension to the myocardium, endocardium, lungs and diaphragm, and metastasis to the liver, brain, adrenal glands and lungs; (2) right pleural effusion; (3) terminal pneumonia; (4) cachexia.

The pathologist's report noted a malignant neoplasm of non-epithelial origin involving multiple organs (Figure 2). The tumor cells had very large

pleomorphic and vesicular nuclei. The cytoplasm varied considerably, in some areas very scant, in others fibrillar, and in still others forming a syncytium with the adjacent cells. The lesion arose from the mesothelial cells of the pericardium and was designated as a malignant mesothelioma, mixed type.

Discussion

Pathologic anatomic characteristics of primary pericardial tumors are¹⁹: (1) Uniform spread in parietal and visceral layers of the pericardium; (2) distension of the pericardium; and (3) hemopericardium.

It is noteworthy that in this case there was multiple distant metastatic involvement of liver, brain, adrenal glands and lungs. According to Dawe and coworkers,⁵ who gathered reports of 25 cases, metastasis occurred in only half of the total number, and multiple distant metastasis in only two. These pericardial tumors have no characteristic clinical manifestations. Certain diagnostic clues, however, may be considered: Congestive heart failure without obvious cause and not responsive to treatment; unexpected modification of cardiac size or rhythm; and appearance of pericardial hemorrhagic effusions.²⁶

Other interesting features of the case herein reported are the early diagnosis by pericardial biopsy and the fact that the first symptoms were those of acute pericarditis with hemopericardium and right heart failure. Early improvement for a period of six weeks followed pericardicentesis and a course of corticosteroids. Adrenal steroids have been advised and found very useful for alleviation of acute symptoms in some patients with non-specific pericarditis. However, recrudescence of symp-

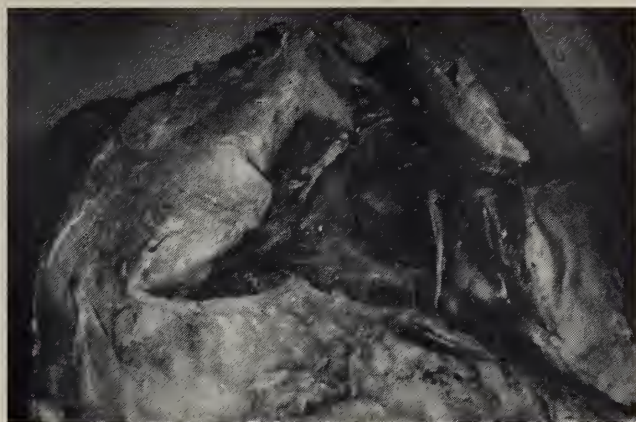


Figure 2.—Pericardial neoplasm enveloping the heart and infiltrating the myocardium.

toms of acute pericarditis occurs frequently with cessation of treatment.⁴

Non-traumatic hemopericardium is most commonly associated with rupture of an infarcted myocardium, rupture of an aortic aneurysm and malignant disease of the pericardium.¹ Other non-traumatic causes of hemopericardium include tuberculosis,¹⁴ uremia,⁸ bacterial endocarditis and myocardial abscess,²⁴ periarteritis nodosa²¹ and non-specific pericarditis.²⁵ There are various ways a malignant pericardial tumor may interfere with cardiac function¹⁸: A cardiac tamponade due to effusion, mechanical constriction of the heart by tumor tissue and interference with the inflow or outflow tracts by encroachment on great vessels passing through the pericardiac sac²³; and interference with the coronary circulation by compression from without by direct invasion and by encroachment of the nerve supply of the myocardium.

Electrocardiographic alterations associated with pericardial tumors have not been well established or differentiated from those associated with myocardial metastasis. The electrocardiographic changes are due to neoplastic invasion of the ventricles, and the changes of pericarditis are often minimal in pericardial malignant tumors.⁹ Oppenheimer and coworkers found a decided lowering of the voltage of the main deflection in all three standard leads.¹³ Electric alternans can also be seen with pericardial effusion, as well as simultaneous alternations of atrial and ventricular complexes.¹⁰ Burchell³ reported on the infrequency of S-T segment elevations in standard leads among patients with pericardial malignancy, while S-T segment elevations are rather frequently found in patients with non-specific pericarditis—a finding pertinent to the present case.

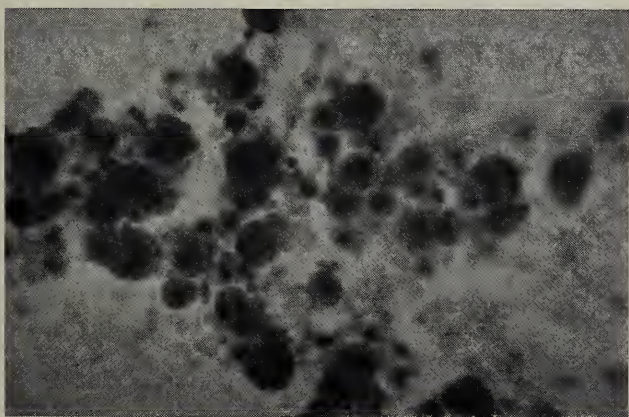


Figure 1.—Cell block section showing clusters of mesothelial cells ($\times 1400$).

There are current indications for pericardial biopsy: (1) Chronic or recurrent pericarditis of uncertain etiology; (2) unexplained hemopericardium, and (3) possibly constrictive or adhesive pericarditis.¹⁷

In the present case the early diagnosis by pericardial biopsy was of no ultimate benefit to the patient, and the chemotherapy was of questionable value.

Summary

A case of primary malignant mesothelioma of the pericardium is reported. The case would appear to support the rationale of early open pericardial biopsy in refractory pericarditis where diagnosis cannot be established by other means.

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Eye Damage in Newborns From Use of Strong Silver Nitrate Solutions

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San Francisco

AFTER MORE THAN a decade of controversy, silver nitrate solution is still the most widely used prophylactic agent for preventing gonorrheal ophthalmitis in the newborn. In March of 1966 the California State Department of Public Health noted⁷ that nine cases of gonorrheal ophthalmia had been reported in three and a half months, a reminder that the disease is not extinct. In 1 per cent concentration, silver nitrate is probably the safest and most efficacious agent for the Crede procedure.¹ However, ocular damage resulting from misapplication of other silver nitrate concentrations has been reported by Dieckmann,³ Lehrfeld⁵ and Davidson and coworkers.² Two cases of permanent and severe eye injury following the accidental substitution of ammoniacal silver nitrate solution (25 to 35 per cent) for the 1 per cent strength are reported herein.

These cases may be unusually significant in the context of a recent decision which could in-

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The material has been reviewed by the Office of The Surgeon General, Department of the Army, and there is no objection to its publication. This review does not imply any indorsement of the opinions advanced or any recommendations of such products as may be named.

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crease a potential hazard for every infant delivered in the State of California. In September 1965, the State Department of Public Health informed health officers and hospital administrators throughout California that the Department would no longer supply silver nitrate solution in wax ampoules "to persons engaged in the practice of obstetrics or assisting at childbirth." This decision appears to be based on a desire of the Department of Public Health to eliminate a function which, although not very costly to the state, could be left to the using medical facilities.

Continuing centralized procurement of ophthalmic silver nitrate, although no longer required by law, might reduce a hazard which few California physicians suspect. When the author saw the first of two infants with ocular damage from too strong a solution of ammoniacal silver nitrate, it seemed unlikely that he ever would see another. That he did, gives both of them extraordinary significance.

CASE 1.—In August 1951 a term male infant, weighing 7 pounds 7 ounces, was delivered following an uneventful pregnancy. The infant appeared normal. About seven hours later he was noted by nursery attendants to have severe redness and swelling of both eyelids and a purulent ocular discharge. A pediatrician examined the infant and recognized that the eye inflammation was too severe to attribute to any common infection so soon after a normal birth. Saline and boric acid irrigations and compresses were used liberally. An ophthalmologist was consulted, and topical treatment of the inflamed conjunctivae was given with cortisone ointment and antibiotics.

Dark brown stains on one eyelid and the cheek suggested chemical injury. Investigation revealed that the only silver nitrate present in the delivery room was packaged in brown glass ampoules which bore the label "silver nitrate solution, ammoniacal." This is a dental caustic, commonly dispensed in 25 to 35 per cent strengths. *But the strength is not stated on the label.*

Fortunately the discovery that this potent solution had been erroneously substituted for the traditional, single-dose, wax ampoules of 1 per cent silver nitrate was made before it could be used on other infants. At least four medically trained persons had had opportunity to detect this substitution but had not recognized the error. Investigation determined that the error originated with the hospital pharmacy.

The infant was observed and treated by the ophthalmologist for a prolonged period. The ini-

tial injury included corneal opacity of the left eye and severe inflammation of both conjunctivae. Partial scarring of the left cornea persisted and there was decided reduction of visual acuity of that eye.

CASE 2.—A term male infant, weighing 7 pounds 3½ ounces, was delivered at home in October 1960, following precipitous labor. The mother and infant were examined in the home by a physician, then were taken by ambulance to a nearby dispensary. No abnormalities were found in either patient and the unattended delivery had been without apparent complications. A physician instilled silver nitrate into both of the infant's eyes. The baby responded with cries of pain and the physician "immediately washed the eyes with a constant sterile saline flush for five minutes to both eyes."

Five hours after delivery, the infant was noted to have pronounced swelling of both eyelids and a seropurulent conjunctival discharge. Irrigations with saline solution were again used and polymyxin-neomycin-bacitracin ophthalmic ointment applied. The infant was transferred to the "suspect nursery" of a nearby hospital. Bacterial conjunctivitis was suspected because of the unsterile delivery, and penicillin and streptomycin were administered parenterally.

The presumed infectious conjunctivitis did not improve with topical therapy. The next day cultures of pus from the eyes revealed a mixed infection of *Aerobacter aerogenes*, diphtheroids and coagulase-negative staphylococci. The infant showed no signs of illness except chemosis and purulent ocular discharge. At first, adequate inspection of the corneas was impossible. Three days later, a consulting ophthalmologist described the infant as having decided mucopurulent conjunctivitis, keratitis and corneal opacity of the left eye. The right eye was felt to show "slight involvement."

The true cause of the conjunctivitis was not recognized until ten days after delivery. After anti-infectious therapy failed, hospital physicians asked the dispensary personnel to review the events subsequent to delivery. Only then was it recognized that ammoniacal silver nitrate (25 to 35 per cent) had been substituted in the emergency obstetrical kit for the wax ampoules of 1 per cent silver nitrate solution. A pharmacy had issued the dental preparation of silver nitrate when unable to supply the wax ampoules.

After six weeks, the infant was transferred to

Letterman General Hospital for further care. Diagnoses listed on the record cover sheet at that time included: "(1) Burn, chemical, left eye. (2) Opacity, cornea, left. (3) Ulcer, cornea, left. (4) Blepharitis, left. (5) Conjunctivitis, left. (6) Symblepharon, left. (7) Entropion, cicatricial, left."

On the advice of several ophthalmologists, definitive surgical correction of the conjunctival and corneal lesions of the left eye was not attempted until the child reached age two years. In 1963, 1964 and 1965, nine separate plastic surgical procedures were carried out in an attempt to restore function and improve the appearance of the left eye. At the most recent examination, the eye had no useful vision.

Discussion

Silver nitrate solution in 1 per cent concentration is well established as an effective agent in prophylaxis of ophthalmia neonatorum. There are no reports of lasting eye damage from this strength of silver nitrate. Mathieu⁶ reported a comparative study in which 2 per cent silver nitrate solution and oxytetracycline were used for gonorrheal prophylaxis and observed no lasting effects of either drug at a follow-up examination six weeks after delivery. Thus, it appears that at least twice the usual concentration of silver nitrate is safely tolerated by infant eyes. Reports of corneal and conjunctival damage due to silver nitrate solution have, without exception, followed the use of this chemical in 5 per cent or greater concentrations.

Harrison⁴ described the action of silver nitrate as follows: "When a 1 per cent solution of silver nitrate is applied to mucous membrane of the eye, the protein in the tissue is coagulated or precipitated by the chlorides present in the tissues. This produces alterations in the permeability of the superficial cells so that there is decreased secretion. The silver chloride produced is an antiseptic and since it is precipitated in the superficial layers, its action is not transitory, and its effects may last several days."

This description of the pharmaceutical action of silver nitrate on the ocular mucous membrane might also imply that a beneficial decrease in permeability to bacterial organisms results from the Crede procedure. The successful use of 1 per cent silver nitrate in the eyes of millions of babies attests the safety of the superficial amount of protein

coagulation. Persistence of antibacterial activity or favorable alteration of the mucous membrane epithelium has not been claimed for one-dose antibiotic ointments or solutions.

The two cases reported here of eye injury from ammoniacal silver nitrate may indicate a particular hazard for babies born in medical installations of the U.S. Armed Forces. Many military hospitals have under one roof both dental and medical facilities which share the same pharmacy. However, it seems reasonable to assume many other circumstances that might lead to substitution of stronger silver nitrate solutions could exist in any hospital. When a pharmacy is unable to supply the obstetrical service with 1 per cent silver nitrate in wax ampoules, a possibility of disastrous substitution exists. The larger the hospital, often the more overburdened is the pharmacy. It is not uncommon for persons other than licensed pharmacists to be given the actual responsibility of taking medications from a stock-room shelf and delivering them to a ward or clinic. Although in the cases here reported, several professional personnel had an opportunity to detect this hazard before it could harm an infant, they did not recognize the error.

Familiarity with the traditional wax ampoule of 1 per cent silver nitrate is not sufficiently widespread among medical personnel. When interns who had just completed their obstetrical rotation at this hospital were questioned recently, it was found that some had never given the Crede prophylaxis during either their internship or clinical clerkship. They did not know that only the wax ampoules should be used.

Ironically, although single dose wax ampoules cannot be permanently labeled individually, practically no other medication in popular use is similarly packaged. Proper identification of these ampoules must depend upon the container in which they are issued rather than the ampoules themselves. Thus, the safety paradox which requires that persons caring for newborn infants reject for ophthalmic use any silver nitrate ampoule which bears the name of the drug.

Subject to the most stringent requirements of quality control and labeling, manufacturers engaged in interstate commerce are the logical source of mass-produced items of single-dose size. They sell ophthalmic silver nitrate solution, 1 per cent, in wax ampoules, to the Federal Government for \$1.80 per package of 24 units. Other users of



Figure 1.—Ampoules of 1 per cent silver nitrate (wax) and 35 per cent dental preparation (amber glass), showing total lack of similarity of appearance.

large quantities should be able to obtain similar low prices.

Centralized procurement, on a statewide scale, of silver nitrate solution has probably spared many California babies ocular damage. Should not familiarity with one packaging of the safe solution be insured by every means possible? Figure 1 shows containers that it would seem could not have been confused, but were. If the state does not continue this protection, is there not another organization with professional concern sufficient to assume this responsibility and modest expense? Direct dispensing from a central source to obstetrical services, by-passing the possibility of pharmacy error, might be a worthwhile added safety precaution.

Summary

Two cases of permanent ocular damage due to accidental application of ammoniacal silver nitrate (25 to 35 per cent) in the newborn period are reported. The accidents illustrate a hazard deserving timely consideration, associated with the California State Department of Public Health's discontinuance of its practice of supplying silver nitrate solution in wax ampoules for lavage of newborn babies' eyes.

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Haemophilus Influenza Type b Orbital Cellulitis

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IN CHILDREN, orbital cellulitis, an inflammation of the cellular tissues of the orbit, is usually an extension of bacterial infection of the paranasal sinuses.⁵ *Streptococci*,⁴ *Staphylococci* and *Escherichia coli*⁶ have been implicated etiologically. Reports of only three cases of orbital cellulitis due to *Haemophilus influenzae* type b have appeared in the English language literature.^{1,3}

During November and December 1965 three children with orbital cellulitis were admitted to the Childrens Hospital of Los Angeles. In each instance *H. influenzae* type b grew on culture of the blood. The purpose of this paper is to report these three cases and to compare them with the cases of other patients with orbital cellulitis admitted to the Childrens Hospital of Los Angeles during the five-year period 1960-1965.

Reports of Cases

CASE 1.—An eight-month-old Mexican-American boy in whom the diagnosis of Sturge-Weber syndrome had been made was admitted to hospital four hours after swelling and tenderness developed in the right orbital area.

On admission the temperature was 40°C (104°F), the pulse rate 144 per minute, respirations 30 per minute and the blood pressure (Flush method) 100 mm of mercury. The right orbital area was massively swollen and purulent conjunctivitis was present. A hemangioma involved the right side of the face and neck. Except for generalized hypotonia no other abnormalities were noted on physical examination.

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Submitted 22 December 1966.

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The hemoglobin content was 10.4 gm per 100 ml of blood. Leukocytes numbered 28,400 per cu mm. Bleeding and clotting times were within normal limits, as were results of urinalysis. The cerebrospinal fluid contained one red cell and three white cells per cu mm, and the sugar and protein content were 75 mg and 20 mg per 100 ml, respectively. *H. influenzae* type b was cultured from the right conjunctival exudate, from the nasopharynx and from the blood. No organisms grew on a culture of the cerebrospinal fluid.

Paranasal sinus roentgenograms demonstrated soft tissue swelling around the right orbit, which obscured the maxillary sinus.

Initial therapy consisted of methicillin 400 mg and ampicillin 300 mg intravenously every six hours. The temperature returned to normal within 12 hours and methicillin was discontinued when the culture reports were obtained. Ampicillin was continued intravenously for 72 hours and then was given by mouth. Swelling, tenderness and redness subsided 72 hours after therapy was begun and the orbital cellulitis subsequently cleared.

CASE 2.—A three-year-old Caucasian boy was well until an upper respiratory infection, without cough or fever, developed two or three days before admission to hospital. On the day of admission fever and swelling of the right eye developed. At this time bilateral haziness of the maxillary sinuses was observed in roentgenograms of the paranasal sinuses. A diagnosis of periorbital cellulitis and sinusitis was made and he was admitted to the hospital.

On admission, the temperature was 38.3°C (100.7°F), the pulse rate 85 per minute and respirations 20 per minute. The right eyelids were swollen, warm and purple. Because of massive edema, the right eyelids were separated with difficulty. No other physical abnormalities were noted.

The hemoglobin content was 14.5 gm per 100 ml of blood and leukocytes numbered 27,000 per cu mm. The cerebrospinal fluid contained 46 red cells and one white cell per cu mm. Sugar content of the fluid was 75 mg and protein content 22 mg per 100 ml. No pathogens grew on a culture of cerebrospinal fluid. A blood culture grew *H. influenzae* type b; and *Neisseria catarrhalis*, *Micrococcus* and *Diplococcus pneumoniae* grew on culture of material from the nasopharynx. Culture of the right conjunctival exudate yielded coagulase negative *Staphylococcus aureus* and alpha *Streptococcus*.

Therapy consisted of intravenous infusion of methicillin, 400 mg and ampicillin 500 mg every six hours for 48 hours. Subsequently ampicillin was given orally. Fever abated within 12 hours, periorbital swelling decreased within 48 hours and the patient recovered.

CASE 3.—The patient was a 19-month-old Caucasian boy in whom upper respiratory infection developed three days before he was admitted to hospital. On the day of admission the parents noted that he was irritable and that the right eyelids were swollen. At the time of admission the temperature was 39.2°C (102.6°F) the pulse rate 120 per minute and respirations 30 per minute. There was extensive edema, warmth and purplish erythema of the right eyelids, cheek and forehead. No other abnormalities were noted on physical examination. Bilateral haziness of the maxillary and ethmoid sinuses was observed on roentgenograms of the paranasal sinuses.

The hemoglobin content was 6.8 gm per 100 ml of blood. Microcytic and hypochromic red blood cells were noted on a smear of blood, and leukocytes numbered 20,800 per cu mm. Results of urinalysis were within normal limits. The cerebrospinal fluid contained eight red cells and one white cell per cu mm, and the sugar and protein contents were 80 mg and 21 mg per 100 ml, respectively. Culture of the cerebrospinal fluid yielded no growth. *H. influenzae* type b grew on cultures of the blood and of material from the nasopharynx, and cultures of exudate from the right eye grew *Klebsiella aerobacter* species, *Micrococcus gamma Enterococcus* and *Diplococcus pneumoniae*.

The patient was treated at first by administration of aqueous penicillin 2,000,000 units and methicillin 500 mg every six hours intravenously. After 12 hours, intravenous administration of chloramphenicol 275 mg every six hours was added to this schedule.

The patient became afebrile 36 hours after admission. By 48 hours the periorbital swelling had subsided and the erythematous areas had become darker in color. Methicillin was discontinued on the third hospital day and on the fifth day penicillin and chloramphenicol were given by mouth instead of intravenously. An iron-containing preparation was given for iron deficiency anemia (Fer-insol®, 1.2 ml three times a day). The right periorbital edema had subsided by the seventh day and only the purple discoloration remained. The patient subsequently made a full recovery.

TABLE 1.— *Data on Infecting Organisms Related to Age of Patients in 16 Cases of Orbital Cellulitis, Childrens Hospital, Los Angeles, 1960-1965*

| Organism | Material Cultured | | Age of Patients |
|-------------------------------------------------------|-------------------------------|-------|-----------------------|
| | Nasopharyngeal or Eye Exudate | Blood | |
| <i>Haemophilus influenzae</i> type b..... | 7 | 4 | 8 months to 36 months |
| <i>Staphylococcus aureus</i> coagulase positive | 5 | 0 | 22 months to 7 Years |
| <i>Micrococcus</i> | 4 | 0 | 40 months to 8 Years |

Discussion

Orbital cellulitis due to *H. influenzae* type b occurs infrequently in children. Of the 16 patients with orbital cellulitis (Table 1) admitted to the Childrens Hospital of Los Angeles from 1960 to 1965, seven were infected with *H. influenzae* type b; five with coagulase-positive *Staphylococcus aureus* and four with *Micrococcus*. In four of the seven cases associated with *H. influenzae* type b, blood cultures were positive for that organism. In the three other cases (in which blood cultures were not obtained) *H. influenzae* type b grew on culture of material from the eye or nasopharynx.

The seven patients with *H. influenzae* type b cellulitis were between eight months and 36 months of age. In other reports² most infections due to *H. influenzae* type b were found in infants and children between the ages of two months and 36 months.

The onset of illness was acute in the *H. influenzae* type b group. All patients were in good health until two or three days before entering the hospital. In most cases, illness began with an upper respiratory infection. The sudden onset of pain and swelling of the orbital area which characterizes *H. influenzae* type b cellulitis may help to distinguish it from cellulitis caused by other organisms. Only two of the nine patients with orbital cellulitis of other cause had sudden onset of symptoms.

The characteristic purple discoloration of *H. influenzae* type b cellulitis as described by other observers¹ was noted in four of the cases reported here. However, it was not always present when the patient was first examined. Involvement of the maxillary or the ethmoid sinuses, or of both, was observed in roentgenograms of four of the seven patients with *H. influenzae* type b.

Early in the period covered by this report, patients with *H. influenzae* type b cellulitis were effectively treated with penicillin in combination with streptomycin, sulfonamides or chloramphenicol. In two of the three cases reported here, treatment was begun with ampicillin and methicillin, with good results.

In seven of ten cases of orbital cellulitis noted in children eight months to 36 months of age, the condition was ascribed to infection with *H. influenzae* type b. Hence, for orbital cellulitis in this age group, therapy in the beginning should be directed against this organism.

Summary

Of 16 cases of orbital cellulitis observed at Childrens Hospital of Los Angeles in a period of five years, seven were caused by *H. influenzae* type b and the patients were children less than three years of age. In light of this incidence, it is believed that until the specific etiologic organism is identified, therapy for orbital cellulitis in children less than three years of age should include an antibiotic effective against *H. influenzae* type b.

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EDITORIAL

A New Executive Director

WHEN HOWARD HASSARD—that's "Hap" Hassard—found himself having to give more and more time to his administrative duties as Executive Director of the California Medical Association and less and less to the business and the philosophy of law, which is his true vocation, he came to a decision that must be respected by anyone who is devoted to any profession or any work: He decided for his vocation.

His decision, which he announced to the CMA Council last winter, presented that body with a problem: How could the vacancy caused by his resignation best be filled without interrupting the continuity of programs being carried forward by a vigorous and progressive medical association? Mr. Hassard agreed to stay on in the post until a decision could be made.

After a period of searching and weighing, the Council decided that the best way to carry forward was to appoint a man already thoroughly familiar with all the work and all the physician leaders of the medical association. Robert Thomas, with his recent experience as Associate Executive Director and long tenure as Director of Commissions and Committees—the nerve center of all CMA activities—was deemed the man for the job. CALIFORNIA MEDICINE extends to him its congratulations and its well-wishes.

To Hap Hassard, who as legal counsel will continue to be readily available for consultation and advice, we acknowledge a debt for the cogent

influence his strong administrative leadership and sound legal guidance has had in the California Medical Association and California Blue Shield. We are grateful to him for giving so much of himself, for being so much a part of us during our time of most vigorous growth and dynamic action.

Planning and Goals in Continuing Medical Education

THE PHYSICIAN'S ROLE in the care of the sick has traditionally been a personal one: the doctor and his patient have represented the unit in good medical care. In spite of the fragmentation of physicians by specialization, the impact of new technology, changes in the pattern of the delivery of health services or a different social order, it seems unlikely that this unit will be any less desirable in the future for good medical care. In such a unit, the personal investment that a physician and a patient make in each other through the years is great and plays a prominent role in any therapeutic action. Much of the "art" of medicine probably arises from this slowly accrued, mutual investment account and, as such, resists measurement. The science that the physician brings to bear and through which he earns the trust of his patients during the years of care is, however, susceptible to appraisal. It is the fantastic explosion of such scientific knowledge that has forced the physician to pursue more diligently than ever before a program of continuing education.

In California the time has come to define some problems and to take action where it seems appropriate. With this in mind, a conference was held on 11 March 1967, at the Hotel del Coronado in San Diego, California. The conference was sponsored by the California Medical Association, under the direction of the California Medical Association Committee on Continuing Medical Education. Support and advice came from the California Medical Education and Research Foundation and the United States Public Health Service. Approximately 100 physicians, medical educators and persons involved in health care were present. These conferees were challenged to come up with specific recommendations for the California medical profession that could be implemented and turned into an action program for continuing education. Four areas were outlined for discussion. These were:

1. The role of the community hospital staff in continuing education; What ways can in-hospital education be improved? What techniques are there to achieve liaison with university medical centers?

2. The evaluation of courses in programs in continuing education and their effect upon the quality of care rendered by physicians.

3. Motivation; Recommendations and plans for achieving greater participation by physicians in continuing education ("CONTINUING EDUCATION" to be defined as courses, assemblies, teaching assignments, journal clubs, etc.). Should there be a system for reaccrediting physicians?

4. Certification of postgraduate courses in continuing education; Should there be such certification? What groups should carry out these duties?

The members of the Conference met in small workshops for detailed discussions and decisions. These decisions in turn were discussed before the full conference, modified and approved. These final recommendations have been approved by the Scientific Board of the California Medical Association and the Council of the California Medical Association. It is proposed now to print the discussions and decisions reached by each workshop. These will appear in this and future issues of CALIFORNIA MEDICINE.

Your comments are encouraged and invited.

DONALD W. PETIT, M.D.
*Chairman, Committee on
Continuing Medical Education
Scientific Board*



California Medical Association



NOTICES AND REPORTS

Robert Thomas Is New CMA Executive Director

ROBERT L. THOMAS was named executive director of the California Medical Association at the July meeting of the CMA Council in Los Angeles.

Thomas, 43, has been an associate executive director of the CMA since March 1966, and a member of the staff since 1951.

He succeeds Howard "Hap" Hassard, who resigned in order to devote full time to his law practice. Hassard has been executive director on a part-time basis since 1958. His law firm has represented CMA for more than a half century. He has been chief counsel to CMA since 1945.

"I regret that the growth of the organization made it necessary for me to choose between being legal counsel and executive director," Hassard said.

"I think we have the best staff of any medical



ROBERT L. THOMAS

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association in the country, and I look upon the Council's action as a vote of confidence in us all," Thomas said in accepting the appointment. "We will continue to contribute our combined efforts to promote the programs and effectiveness of the association."

Thomas was graduated from the University of California at Berkeley in 1948 with a degree in business administration, and is a graduate of the

American Institute of Organizational Management. He is an active member of the American Society of Association Executives and American Association of Medical Society Executives.

Council Meeting Minutes

Tentative Draft: Minutes of the 533rd Meeting of the Council, San Francisco, Hilton Inn, 27 May 1967.

The meeting was called to order by Chairman Miller at the Hilton Inn, on Saturday, 27 May 1967, at 9:30 a.m.

A quorum was present and acting (full roll call, including names of invited guests, appears in Item 34).

1. Election of New Fourth District Councilors

On behalf of the Council of the Los Angeles County Medical Association, Vice-Speaker Boyle recommended the election of Sam S. Woolington, M.D., of Long Beach and Robert L. Watson, Jr., M.D., of Los Angeles to fill the vacancies in the Councilor offices held by President-Elect Todd and Vice-Speaker Boyle.

ACTION: Voted to elect Sam S. Woolington, M.D. and Robert L. Watson, Jr., M.D. as new Fourth District Councilors, to serve as provided in Chapter VIII, Section 9 of the Bylaws.

2. Minutes for Approval

The minutes of the 531st Meetings of the Council, held 14 to 19 April 1967, and of the 532nd meeting held 19 April 1967 were approved.

3. Report of the President

President Morrison read a letter recently received from Doctor Dwight L. Wilbur, Editor of CALIFORNIA MEDICINE. Doctor Wilbur stated that it was his understanding that the election of an Associate Editor for CALIFORNIA MEDICINE would be brought before the Council by the end of summer.

Doctor Morrison also gave a progress report on the CMA-Blue Shield Congressional Visitation, scheduled for 15 and 16 June in Washington, D.C. He stated that the function would enable the

visiting group to meet with California Congressmen, Senators and their staff on an individual basis as well as in group sessions. Doctor Morrison recommended that the Council approve himself and Doctors Miller and Boyle to represent CMA on this trip.

ACTION: Voted to approve Doctors Morrison, Miller and Boyle to represent CMA on the Joint Congressional Visitation.

Doctor Morrison mentioned that Blue Shield would be represented by Doctors Richard Wilbur, Carl Anderson and Gregory Murray.

Doctor Morrison called the Council's attention to the proposed bylaws for implementing the Council's previous decision to participate in a joint data collection project with the California Hospital Association. The Council reviewed the proposed bylaws for the "California Health Data Corporation" as well as the outline of data to be collected for each patient. There was some discussion regarding whether the organization should be designated as a "Corporation" or "Foundation." Gordon R. Cumming, president-elect of the California Hospital Association, generally explained how the proposed organization would operate. It was pointed out that Article IV of the proposed bylaws would not legally bind CMA to any sizeable contribution to the organization without Council approval.

ACTION: Voted to approve the proposed bylaws for the "California Health Data Corporation," with the understanding that the Committee for Emergency Action, in concert with the Executive Committee of the California Hospital Association, would be authorized to make such changes as necessary as the project progresses.

Doctor Morrison also commented briefly on a number of meetings he had recently attended or planned to attend, representing the CMA. Among these was a projected meeting with Governor Reagan and his staff. Doctor Morrison stated that he hoped this meeting would result in the development of a continuing liaison with the Governor's office regarding matters affecting the public health.

4. Report of the President-Elect

President-Elect Malcolm C. Todd reported on various meetings he had recently attended, including meetings with representatives of the California Licensed Vocational Nurses, the Southern California State Dental Association, the California Hospital Association, the Public Health League and the Hospital Planning Association of Southern California.

5. *Committee on Committees Recommendations*

On behalf of the Committee on Committees, President-Elect Todd recommended that the ad hoc Committee to Study Relations of CMA with Component Medical Societies be disbanded. It was pointed out that the activities of this committee would be continued by the Committee on Organizational Review and Planning.

ACTION: *Voted to disband the ad hoc Committee to Study Relations of CMA with Component Medical Societies, with thanks.*

President-Elect Todd also asked Council approval for transferring the Subcommittee on Long-Term Care Facilities from the Commission on Public Agencies to the Commission on Hospital Affairs, charging the subcommittee with the additional responsibility of maintaining liaison with the California Association of Nursing Homes.

ACTION: *Voted to approve the above changes for the Subcommittee on Long-Term Care Facilities.*

Doctor Todd recommended that there should be listed a Committee on Drugs composed of the membership of the Committee on Adverse Drug Reactions and the Committee on Dangerous Drugs, with William F. Quinn, M.D., as Chairman. The other two committees would be titled subcommittees.

ACTION: *Voted to approve the above suggestions regarding the formation of a Committee on Drugs.*

Chairman Miller, on nominations presented by the Committee on Committees and the Council concurring, made the following appointments:

Commission on Communications—Elmer F. Gooel, M.D., Beverly Hills, as Chairman.

Commission on Public Agencies—William F. Kaiser, M.D., Berkeley, as Chairman.

Committee on Public Health—William F. Kaiser, M.D., Berkeley.

Committee on Organizational Review & Planning—James H. Yant, M.D.

Council ad hoc Committee on Specialty Conference (reapportionments)—Glenn A. Pope, M.D., Chairman, Sacramento; Rodney R. Beard, M.D., Palo Alto; William R. Foster, Jr., M.D., Los Altos; Charles E. Grayson, M.D., Sacramento; John S. Hattox, Jr., M.D., San Diego; William F. Kaiser, M.D., Berkeley; J. J. McCort, M.D., San Jose; J. Blair Pace, M.D., Oceanside; Homer C. Pheasant, M.D., Los Angeles; Keith P. Russell, M.D., Los Angeles.

Committee on Fees—Nelson Keeler, M.D., Oakland, as Consultant.

Medical Advisory Committee to the State Department of Rehabilitation (recommendations)—Gregory Bard, M.D., San Francisco; Walter J. Gillogley, M.D., San Mateo; Jerome R. Klingbell, M.D., Long Beach; Vernon L. Nickel, M.D., Downey; Howell E. Wiggins, M.D., San Diego; Edward Zaik, M.D., Los Angeles.

California Health Data Corporation (Board of Directors)—James C. MacLaggan, M.D., San Diego; Glenn A. Pope, M.D., Sacramento; Dexter N. Richards, Jr., M.D., Oakland; Robert Stragnell, M.D., Arcadia; Albert E. Warrens, M.D., Chico.

Bureau of Research and Planning—Henry V. Eastman, M.D., Tustin.

Committee on Mediation—Harold A. Neibling, M.D., Long Beach.

Committee on Environmental Health—Grace M. Talbott, M.D., Chairman, San Francisco; Elmer P. Halley, M.D., Stockton; Kenneth Smith, M.D., South Tahoe.

Commission on Community Health Services—Grace M. Talbott, M.D., San Francisco.

Committee on Federal Medical Care Programs—Samuel S. Woolington, M.D., Long Beach.

Liaison Committee to CMAA—Eugene Clement, M.D., Castro Valley, as Consultant.

Council Advisory Committee to CMA Representatives to the California Committee on Regional Medical Programs—Jean F. Crum, M.D., Downey.

CMA Representative on State Department of Public Health "Advisory Committee on Social Care"—Joseph P. O'Connor, M.D., Pasadena.

Tulare County Hospital Survey Team—William L. Argo, M.D., Chairman, Fresno; Ralph W. Burnett, M.D., Bakersfield; John R. Heckman, M.D., Marysville; John T. Saidy, M.D., San Mateo.

6. *Professional Liability Insurance Survey*

In the absence of Doctor George Herzog, chairman of the Commission on Professional Welfare, Mr. William Whelan briefly commented on the draft of the proposed form for a survey on professional liability, to be conducted by the Bureau of Research and Planning for the CMA Medical Review and Advisory Committee. Councilor Kaiser stated that Doctor Goetsch, a member of the Medical Review and Advisory Committee, had some reservations regarding the proposed survey form and suggested that it be referred back to the com-

mittee for further consideration. After some discussion, it was suggested that the Council approve the survey, contingent upon Doctor Yant, chairman of the committee, and Mr. Whelan consulting with Doctor Goetsch regarding his suggestions.

ACTION: *Voted to authorize the Bureau of Research and Planning to proceed with the survey (Doctor Goetsch's suggestions to be taken into consideration).*

7. Keogh Plan Changes

Two proposed changes in the California Medical Association Members' Retirement Plan and Trust (Keogh) were offered for Council consideration by the Commission on Professional Welfare. Mr. Whelan commented on the proposed changes, which were:

a. the addition of two mutual funds as optional investment vehicles (The Fidelity Group which includes Fidelity Fund, Puritan Fund, Fidelity Capital Fund and Fidelity Trend Fund; and the Commonwealth Group which includes the Commonwealth Investment Company, Commonwealth Stock Fund, Commonwealth Income Fund and Commonwealth Capital Fund).

b. the amendment of the plan to provide for the establishment of a voluntary contribution account by both the employer and his employees when they so desire.

Mr. Whelan explained that the Keogh Law provides for the establishment of such voluntary accounts and furnishes a shelter from taxation of the income and growth earned during the time the funds are kept in such a voluntary account.

ACTION: *Voted to approve the proposed changes in the CMA Members' Retirement Plan and Trust (Keogh).*

8. Annual Session Planning

Five suggestions for scheduling of future Annual Sessions were submitted for Council consideration by Mr. Hassard. The suggestions were:

a. Annual Session should be planned five years in advance, with firm sites and dates.

b. It should alternate between San Francisco and Los Angeles, each year, until new cities with adequate facilities can be worked into the schedule.

c. It should be scheduled earlier in the year, preferably during the month of February and no later than mid-March.

d. Some flexibility should be exercised in establishing the one-to-one ratio in the meeting location.

e. A staff site selection committee should be appointed by the Executive Director (to be composed of the staff coordinator for the Scientific Board and the staff coordinator of Annual Session).

During the ensuing discussion, it was pointed out that the proposed staff selection committee (item e.) should report to the Speaker of the House, the Chairman of the Council and the Chairman of the Scientific Board. There was some doubt expressed as to whether item c. concerning timing of Annual Session was at variance with any position taken by the House of Delegates. Staff was asked to check into any possible conflict.

ACTION: *Voted to approve the five suggestions regarding scheduling of Annual Session (Item e. as amended and Item c. contingent upon the absence of conflict with any previous House of Delegates position).*

9. Meetings with Component Society Officers

President Morrison discussed the possibility of CMA's sponsoring two or three small, relatively informal meetings with presidents of component societies including presidents of LACMA districts—similar to the breakfast meeting held on 17 April 1967, in conjunction with Annual Session. Doctor Morrison explained that the meetings would stress dialogue rather than formal presentations. He suggested that this year such a series of smaller but state-wide meetings might be substituted for the traditional Component Society Officers Conference—on a trial basis. Several Councilors, including Doctors Boyle, MacLaggan and Eastman, voiced their support of the idea of holding the smaller meetings, but registered opposition to deleting the Component Society Officers Conference from this year's schedule of meetings. It was suggested that the Council might want to consider changing the time of this year's Component Society Officers Conference to autumn, rather than January.

ACTION: *Voted to approve holding two or three smaller meetings with component society presidents as well as the Annual Conference of Component Society Officers during 1967 (the subject of timing for the annual conference to be considered at the 8 July 1967, meeting of the Council).*

During the discussion on the above topic, Doctor MacLaggan mentioned the importance of com-

ponent society officers having special identifying name tags for CMA Annual Sessions.

10. *Reports from Medical Schools*

Councilor James Yant reported for Dean Tupper of UC School of Medicine at Davis, who was unable to attend the Council meeting because of an emergency meeting at his school. Doctor Yant reported that progress at the school is again on schedule and expressed Doctor Tupper's thanks for his appointments to CMA committees.

Dean Stuart Cullen of UC School of Medicine in San Francisco reported that his school had recently received its Regional Medical Program grant under the Heart Disease, Cancer and Stroke legislation. He also announced that the school now had official affiliation with Letterman General Hospital and Children's Hospital; it is negotiating for affiliation with Franklin Hospital and Mount Zion Hospital.

Dean Warren Bostick of UC-California College of Medicine reported that the decision to locate the UC-CCM Campus at Irvine in Orange County was facilitating recruitment of new faculty. He stated that the move was necessarily being accomplished in planned stages, but was being carried out as rapidly as possible.

11. *Health and Welfare Agency*

Mr. Carel E. H. Mulder, director of the Office of Health Care Services, directed his remarks to the history and current status of the Medi-Cal program. He pointed out that it was just ten years ago in June that the State Legislature had passed the first Public Assistance Medical Care Program, which received support from CMA in that it contained three basic principles: (a) free choice of physician, (b) payment on a "fee for service" basis, and (c) the use of a fiscal intermediary. Mr. Mulder pointed out that the current Medi-Cal program contains these same principles—strengthened. Medi-Cal, he reminded the Council, is designed to extend freedom of choice so that lower-income patients are brought into the "mainstream," to substitute "usual and customary" fees for an arbitrary fee schedule, and to utilize a state-wide fiscal intermediary—Blue Shield. He warned, however, against complacency, pointing out that each of these principles is now in danger and should be implemented more fully. He stated that we need to have more physicians participating in the pro-

gram to make freedom of choice a reality. And there is real concern, he said, regarding the method of paying physicians; although those who would doubt the feasibility of the "usual and customary" approach may base their opinions on misconceptions, still they must be convinced that the method is truly workable and desirable.

Regarding the fiscal intermediary concept, Mr. Mulder stated that various aspects of handling the program—medical auditing, speed of payment and determination of eligibility—need further improvement. He concluded by assuring the Council that the Office of Health Care Services stands ready to work with physicians and others in keeping principles underlying Medi-Cal a reality.

12. *Social Security Administration*

Mrs. Mercia Kahn, regional director of the Bureau of Health Insurance, Social Security Administration, reported on current developments concerning the Medicare program. She stated that the list of approved laboratories continues to grow, with 525 now certified for payment under Medicare. Because changes occur so rapidly, Mrs. Kahn urged physicians to rely on the laboratories themselves, the carrier or the local district Social Security offices when they are in doubt regarding the status of a given laboratory. She also stressed that the number of approved extended care facilities has been growing rapidly. In May, she stated, 20 more facilities representing 1,402 beds were added. Mrs. Kahn also gave some cumulative statistics on Part B of the Medicare program. From the time the program went into effect through the end of April, she said, twenty million physician and other medical services had been rendered under the program, constituting \$434 million in payments. Of this amount, \$74.5 million (or over 17 per cent) was in California. Ninety per cent of the Part B bills, she said, were for physicians' services, but 40 per cent of these required no payment because of the deductible. Mrs. Kahn said she would find out for the Council what the breakdown was in dollars between physicians and "other services."

She also reported that the carriers are continuing to increase their capacity to process claims more rapidly. One major problem is that the percentage of bills which have to be returned because of incomplete or incorrect information is rising. The main reason for this, she said, is that the Social Security Health Insurance number is often inaccurate or missing. She reminded the Council

that the local Social Security offices are available to help in determining correct numbers.

13. *State Department of Mental Hygiene*

Director James Lowry was represented by Doctor E. F. Galioni of the State Department of Mental Hygiene. Doctor Galioni commented briefly on the new budget for the Department, which, he said, calls for a reduction in personnel commensurate with the drop in patient population. These changes would result, he said, in the Department's starting the fiscal year with about 100 personnel related to direct treatment for every 255 patients. He stated that there were currently about 1,000 vacancies in all classes of personnel to be reduced and that by July 1967 approximately 700 more were scheduled for reduction.

14. *State Department of Rehabilitation*

Representing the State Department of Rehabilitation, in the absence of Director Robert E. Howard, Doctor Richard Young thanked the Council for its interest in the progress of the Department's activities and expressed his hope that this interest would continue. He also expressed his appreciation to the Council for appointing members to serve on a medical advisory committee to the Department.

15. *California Hospital Association*

Mr. Gordon Cumming, President-Elect of the California Hospital Association, announced the completion of the "Arthur Young Report"—an objective study of a cross section of California hospitals in relation to reimbursement under Medicare. Mr. Cumming said that the report shows that the great majority of hospitals receive less than their charges and realistic costs under Medicare, impairing their ability to continue present services or to expand. He assured the Council that the CHA is taking a position of leadership in urging revision of the Federal formula.

President-Elect Todd suggested that CMA express its support for CHA efforts to modify the reimbursement formula under Medicare.

ACTION: *Voted to support the California Hospital Association in its efforts to revise the reimbursement formula for hospitals under Medicare.*

Mr. Cumming announced that CHA had recently received a \$45,000 grant under Public Law 89-239 (Heart Disease, Cancer and Stroke Legislation) to conduct regional meetings in coopera-

tion with the California Committee on Regional Medical Programs and the CMA. A series of 12 meetings in relatively non-metropolitan areas are planned, he said, with the first scheduled to be held in Modesto on 21 June.

He also commented on the importance of CMA's participating in guiding the implementation of Public Law 89-749 (Comprehensive Health Planning and Public Health Service Amendments of 1966) in California. He said that the CHA was making efforts to have a voice on the Council which will advise Doctor R. Leslie Smith, Regional Director of the U.S. Public Health Service.

Concluding his remarks, Mr. Cumming said that the CHA was following the example of CMA in setting up a committee responsible for long-range planning so that CHA might better meet its growing responsibilities to the public.

16. *California Veterinary Medical Association*

Doctor William Stansbury, president-elect of the California Veterinary Medical Association, said that the major problem facing his organization is educating enough veterinarians. He commended Councilor Bullock for his assistance in solving this problem. The Association is working diligently for the creation of another veterinary medical campus in the State, he concluded.

17. *California Nurses' Association*

Mrs. Helen Hancock, president of the California Nurses' Association, thanked CMA for inviting nurses to the CMA Annual Session. She reported that CNA membership has doubled during the last year, bringing the current figure to 24,000 members. Mrs. Hancock also commented on the activities of the Health Manpower Council.

18. *California Medical Assistants Association*

Miss Helen Goldman, president of the CMAA, briefly reported on recent activities of her Association. She reviewed CMAA's participation in the CMA Annual Session and the program held in conjunction with the recent CMAA Board Meeting in Monterey.

19. *California Delegation to the AMA*

Doctor Burt Davis, chairman of the CMA Delegation to the AMA, began his report by commenting on the AMA Long-Term Disability Insurance Program problem. He outlined the background of the problem and discussed the study which had been conducted by an independ-

ent actuary at the request of CMA. He said that the written results of this analysis would be made available to the Delegation in advance of the AMA Convention. Discussion followed.

ACTION: *Voted to receive the preliminary report on the AMA Long-Term Disability Insurance Program for information.*

Doctor Davis also previewed the AMA Convention, stating that the Delegation was confident in its belief that Doctor Dwight L. Wilbur would be voted AMA President-Elect. Regarding resolutions, Doctor Davis reported that 14 resolutions were currently scheduled for introduction—12 of these resulting from actions taken by the 1967 CMA House of Delegates.

Councilor Boyle discussed and presented for Council consideration an additional resolution concerning Blue Cross Association President Walter J. McNerney's recent statements regarding organization of medical care. The resolution reads as follows:

Whereas: Blue Cross as an organization is a creature of hospitals, both at the national and at the local level; and

Whereas: Hospital administration and Blue Cross are primarily involved in hospital management and not in the private practice of medicine; and

Whereas: Mr. Walter McNerney, President of the Blue Cross Association, recently came forward with the statements in a press release entitled "Blue Cross President Predicts Spread of Group Practice, Greater Controls and Planning to Curb Health Cost Rises"; and

Whereas: Wide publicity was given to his statements such as ". . . (Mr. McNerney) embraced the group practice of medicine to help reduce the spiraling cost of health care and ease the shortage of doctors and nurses"; now, therefore, be it

RESOLVED: That the Board of Trustees of the American Medical Association negotiate with the American Hospital Association in an effort to get its subsidiary organization, Blue Cross, to confine its activity to that of hospitalization and restrict it from making public statements relating to the private practice of medicine and which are of concern to physicians and physician organizations who are truly qualified to advise the American public in a reliable and constructive manner; and be it further

RESOLVED: That the American Medical Association oppose the use of any federal funds or

grants of any type of any sort to be used by Blue Cross to undertake any studies where the objective is to evaluate the delivery of professional medical services to the American public.

ACTION: *Voted to transmit the above resolution to the CMA Delegation to the AMA.*

20. Finance Committee

Chairman Harold Kay first reviewed requests submitted to the Finance Committee which had been declined. He then presented proposed changes in CMA policy regarding honorariums. The first change involved elevation of honorariums for the President and President-Elect.

ACTION: *Voted to raise honorariums for the President and President-Elect to \$200 (in addition to the per diem) for time spent away from their practice on any day, when acting or traveling in an official capacity.*

The second proposed change in policy on honorariums related to providing for increasing the honorarium for any CMA member under exceptional circumstances.

ACTION: *Voted to extend the payment of a \$200 a day honorarium to any CMA member asked to serve the association under exceptional circumstances if approved by the Committee for Emergency Action and the chairman of the Finance Committee.*

Doctor Kay said that a letter would soon be sent to Officers and Councilors clearly indicating the current CMA policy on Per Diem and Honorariums as well as the new method for submitting expense accounts.

On behalf of his committee, Doctor Kay distributed to the Council a report on delinquent dues as of 15 May 1967. He also reviewed expenditures which have been approved by the Council, but were not in the current fiscal budget, stating that such items amounted to \$93,000. Even though these expenditures were highly beneficial projects which could not be anticipated, he said they cut deeply into surplus funds. Doctor Kay reminded the Council to exercise caution in approving unbudgeted items.

21. Committee on Legislation

Chairman Kilroy informed the Council that the State Legislature, in its 21st week of the 1967 session, had over 4,200 bills under consideration. Of these, in excess of 500 have some effect on the practice of medicine. Doctor Kilroy reported on various bills pending before the State Legislature. A number of these were considered by the Council.

22. *Distribution of "Strengthening Health Care for Californians"*

President-Elect Todd, immediate past chairman of the Commission on Communications, commented on the booklet, "Strengthening Health Care for Californians," which was distributed to the 1967 House of Delegates. The publication was originally designed, Doctor Todd explained, to be sent to approximately 4,000 lay opinion leaders throughout the State—to inform them of some of the many positive contributions CMA makes in the interest of better health care. In response to the House of Delegates' recommendation that this report should receive "the widest possible professional and public exposure," Doctor Todd said that it would be reprinted for distribution to the CMA membership. He reported that the cost would amount to approximately 50 cents per copy, to be taken out of the previously approved Communications budget. By making a copy available to each member, Doctor Todd said, the booklet will serve as a valuable tool for individual public relations efforts by physicians throughout the State.

23. *Referrals of 1967 House of Delegates Resolutions and Recommendations*

Resolutions by the 1967 House of Delegates as well as several Reference Committee Recommendations were reviewed, and recommendations for action or referral to commissions or committees were discussed.

ACTION: *Voted to refer 1967 House of Delegates Resolutions and Reference Committee recommendations (not embodied in resolutions) to various CMA commissions and committees for action or study. (These actions are attached and made a part of these minutes.)*

It was pointed out that the CMA Constitution and Bylaws should be revised to incorporate the Bylaw amendments passed by the 1967 House of Delegates.

ACTION: *Voted to reprint the CMA Constitution and Bylaws, incorporating Bylaw amendments acted upon by the 1966 and 1967 House of Delegates.*

24. *California Blue Shield*

Blue Shield Board Chairman Richard Wilbur reported that so far this year the organization has added 19,000 Blue Shield members and 12,000 California Physicians' Insurance Corporation members—bringing total membership (without duplication) to 1,217,000. He also reminded the Council that the "Major Medicare" program would open

for enrollment on 1 July and that physicians will be receiving two informational mailings on the program in advance of that date. Enrollment will be open through August 1967.

During April, Doctor Wilbur said, \$57 million, representing 3.5 million claims, was paid out by Blue Shield.

Since its inception, Medi-Cal has accounted for \$214 million in payments, representing 17 million claims. Determination of eligibility continues to be a problem, he said. There are currently 188,000 Medi-Cal claims which cannot be paid due to ineligibility. Blue Shield soon will shift the entire responsibility for determination of eligibility to the State.

Under Medicare, Doctor Wilbur stated, some 1.9 million claims have been processed so far, representing \$54.5 million (in California as a whole, about \$74.5 million has been paid).

Doctor Wilbur described current Blue Shield efforts in the field of utilization review. He said that 637 cases had recently been reviewed, and of these, only 12 were found to be real problems. He said that it takes review of a great many cases to determine the few where practice is really "out of line." Blue Shield is designating one computer for use only in utilization review.

At the recent organizational meeting of the Blue Shield Board of Trustees, the following officers were elected: Chairman: Richard S. Wilbur, M.D.; Vice-Chairman: Wilbur G. Rogers, M.D.; Treasurer: Philip S. Magruder, M.D.; Secretary: Gregory C. Murray, M.D.

Doctor Carl E. Anderson was elected to be chairman of the Medical Policy Committee and Doctor Bert Halter was elected chairman of the Finance Committee.

25. *Medical Executives Conference*

Medical Executives Conference Chairman Eldon Geisert stated that his organization's goal during this year was to strengthen its functions so that it might better fulfill its responsibilities of acting in an advisory capacity to the CMA Council and staff and providing a forum for interchange of information and opinions among executive secretaries of component societies.

26. *Position Paper on Drug Abuse*

Mr. Geisert called on Robert Wood, chairman of the MEC Committee on Dangerous Drugs, to give the next portion of the report. Mr. Wood

stated that the medical executives had expressed real concern that the CMA had not spoken out more forcefully regarding use of drugs and presented the following resolution for Council consideration:

"RESOLVED, that the Medical Executives Conference recommends that the Council prepare a position paper on Medicine's attitude toward drug abuse, particularly among adolescents. And further, that this paper be prepared as soon as possible and be given the widest distribution."

Discussion followed, during which it was pointed out that caution should be taken to be sure the resulting paper would be scientifically sound.

ACTION: *Voted to approve the resolution concerning the preparation of a CMA position paper on drug abuse.*

A brief discussion of distribution of the paper ensued. It was suggested that it be sent to all news media as well as disseminated for use in schools throughout the State.

27. *Multiphasic Screening Program for Cannery Workers*

Speaking for the MEC Committee on Medical Services and Insurance, Mr. Howard Pearce discussed the multiphasic screening program to be conducted for cannery workers by Health Testing Services Incorporated. On behalf of his committee, Mr. Pearce presented the following recommendations (as amended) for Council consideration:

a. CMA should continue to study both the quality and appropriateness of such programs.

b. the involved county medical societies should continue to be interested in the programs and to carry out discussions with the program directors,

c. county medical societies which feel that the program has need for local medical guidance should continue to keep each other informed and lend medical guidance to the program, both during the operational and the referral stages and during the interpretation and evaluation stages (in cooperation with the Commission on Community Health Services), and

d. a complete report of the program should be placed before the Council at an appropriate time in the future.

ACTION: *Voted to refer the recommendations to the Commission on Community Health Services for study and report back to the Council.*

28. *Medicare—Medi-Cal Workshops*

Mr. Pearce also presented a recommendation from his MEC committee that CMA sponsor workshops for component societies on Medicare and Medi-Cal, similar to the regional workshops held on June 4-5, 1966. He stated that the workshops could be designed to review the first year's progress and problems under the government programs, to review quality review mechanisms and to review billing procedure practices. During the discussion, it was suggested that the workshops should be regional and that participants should include representatives of local review committees as well as component society officers.

ACTION: *Voted to refer the suggestion to the CMA-Blue Shield Liaison Committee for implementation (Councilors to be encouraged to attend the workshops).*

29. *CalPac Membership*

President-Elect Todd, 1966-67 chairman of CalPac (California Volunteers for Political Action), announced that the following had been elected to CalPac's 1967-68 Executive Committee: Malcolm C. Todd, M.D., Long Beach (Chairman); Joseph P. Cosentino, M.D., Sacramento; Edward T. Kelley, M.D., San Francisco; David B. Kuris, M.D., Los Angeles; James C. MacLaggan, M.D., San Diego; John E. Vaughn, M.D., Bakersfield; Gilbert F. Whipps, M.D., Los Angeles; Milton G. Evangelou, M.D., San Diego; Richard S. Wilbur, M.D., Palo Alto; Merlin A. Hendrickson, M.D., Rialto; Howard E. Wilkins, M.D., Downey; and Mrs. George J. Bower, Redding. Honorary Chairman is Dwight H. Murray, M.D., Napa.

Doctor Todd also briefly reported on the organization's current membership drive. He commended the editorial by Vice-Speaker Joseph Boyle which appeared in the 4 May 1967 *Bulletin* of the Los Angeles County Medical Association. The editorial, he said, constitutes the best statement to date on CalPac. Doctor Todd also mentioned that many component societies are exhibiting renewed interest in building support for CalPac. He urged 100 per cent membership for Councilors. Mr. Bob Garrick of the CalPac staff also urged the Councilors, as leaders of the medical profession in California, to set an example of CalPac support. Mr. Garrick reported that CalPac's 1967 membership figure is 1,080—less than 5 per cent of CMA membership.

30. *Bureau of Research and Planning*

Bureau Chairman Carl E. Anderson, M.D., reported that the Bureau of Research and Planning would be having its next meeting on 7 June. In the meantime, he said, the Bureau has been involved in a number of important activities, including the preparation of a booklet summarizing existing and pending legislation involving federally financed health care. The resulting booklet, "A Compendium of Selected, Current and Pending Legislation (Related to the Provision, Financing, and Organization of Health Care)" was distributed to the Council. The booklet, prepared in response to requests from the Council and the Medical Executives Conference, is being distributed to all component societies. Doctor Anderson pointed out one item of information which should be added to the last section of the summary. HR 6418 (page 62) not only is concerned with the Federal licensing of clinical laboratories, but is an extension of P.L. 89-749 (Comprehensive Health Planning and Public Health Service Act of 1966). On behalf of the Bureau, Doctor Anderson also distributed a document of excerpts from the "Corson Report," which he described as the "blueprint" for implementation of Public Law 89-749. The document spells out the proposed relationships under the Federal legislation, between HEW and state health agencies, as well as health planning councils, among other groups. He urged the Council to study the document.

31. *Report of Legal Counsel*

Legal Counsel Howard Hassard presented a progress report on the lawsuit initiated by the State Employees' Association contending that only the State, through the Civil Service System, can lawfully administer the Medi-Cal program. He said the suit is still pending. The defendants (Blue Shield, Blue Cross and Spencer Williams) have challenged the jurisdiction of the court on the grounds that the State Employees' Association has not exhausted administrative remedies through the State Personnel Board. A hearing on this subject has been set for 12 June in Sacramento.

32. *Schools of Public Health*

Immediate Past President James C. MacLaggan commented on the importance of maintaining liai-

son with the two Schools of Public Health in the State. He said that he had recently attended a conference sponsored by the UCLA School of Public Health at which the role of hospitals and extended care facilities in community medical care was discussed for three and one-half days by over 70 participants. Doctor MacLaggan suggested that the two Deans of the Schools of Public Health regularly be invited to Council meetings.

ACTION: *Voted to approve extending invitations to meetings of the CMA Council to Deans of the two Schools of Public Health.*

33. *Membership*

Thirty-three applicants were voted election to Associate Membership. These were: Edward F. Kelly, Harold E. Patterson, Jr., Stanley L. Sizeler, Lloyd Tom, Alameda-Contra Costa County; Priscilla D. Boekelheide, Butte-Glenn County; Clifford O. Bishop, Elizabeth Christine Costley, Maritza L. Garrido, Everett George, Theodore J. Lynch, David T. Murray, Evelyn M. Myers, Mary O'Callaghan, Robert L. Swezey, Leo Tepper, Roy Lee Walford, Jr., Los Angeles County; Edward Hirschberg, Charles H. McIntyre, Monterey County; Robert D. Allbaugh, Alexander E. Buehler, Donald J. Feerer, Orange County; Alberta R. Bassett, Riverside County; Ernest N. Krueger, Thais V. Thrasher, San Bernardino County; Clyde W. Norman, Shirley J. Phelps, San Diego County; Cedric R. Bainton, Harold J. Hubis, San Francisco County; John Philip Harney, San Mateo County; Dwight Bissell, Charles E. Harman, Joseph G. Toole, Santa Clara County; Lawrence Leo Loughlin, Stanislaus County.

Seven members were voted election to Retired Membership. These were: John M. Murphy, Alameda-Contra Costa County; Arthur Wallace Eaton, Jr., Kern County; Murray I. Sloane, Los Angeles County; Ethel D. H. Priest, Napa County; Kenneth Vernon Powers, Herman Vehrs, Orange County; Earle T. Dewey, San Francisco County.

Reduction of dues was voted for 30 members for reasons of prolonged illness or postgraduate education.

34. *Roll Call*

Present were: President Morrison, President-Elect Todd, Speaker Quinn, Vice-Speaker Boyle, Secretary Weyrauch and Councilors Moore, East-

man, Melone, Woolington, Gooel, Shapiro, Bullock, O'Connor, Pheasant, Rogers, Crum, Watson, Maguire, Burnett, Richard Wilbur, Miller, Watts, Fenlon, Kay, Kaiser, Yant, Grunigen and Immediate Past President MacLaggan.

Present by invitation were CMA staff members Becker, Bowman, E. Collins, J. Collins, Curley, Eberlein, Edwards, Goldman, Hetland, Klutch, Lemos, Miller, Price, Redfern, Thomas and Whelan; Messrs. Hassard and Huber, legal counsel; component society executives Scheuber of Alameda-Contra Costa, Rideout of Butte-Glenn, Garrick of Forty First, Lingerfelt of Fresno, Geisert of Kern, Dalbec of Los Angeles, Sower of Marin, Colvin of Monterey, Searcy of Napa, Walters of Riverside, Dochterman of Sacramento, Donmyer of San Bernardino, Nute of San Diego, Neick of San Francisco, Wood of San Mateo, Marvin of Santa Barbara, Pearce of Santa Clara, Brown of Sonoma and Whitehall of Stanislaus; Messrs. Patton, Koch, Babb, Clark and Heller of California Blue Shield; Messrs. Read, Brown, Putnam and McWilliams of the Public Health League; Doctor Cullen of UC-San Francisco; Doctor Bostick of UC-CCM; Mr. Mulder and Doctor Rosen of the Office of Health Care Services; Doctor Bost of the State Department of Public Health; Doctor Skelly of the State Department of Social Welfare; Doctor Galioni of the State Department of Mental Hygiene; Doctor Young of the State Department of Rehabilitation; Mrs. Kahn and Mr. Olson of the Bureau of Health Insurance, Social Security Administration; Mr. Snyder of the California Society of Pathologists; Doctor Stansbury of the California Veterinary Medical Association; Mr. Cumming of the California Hospital Association; Mrs. Flood of the Woman's Auxiliary to the CMA; Mrs. Hancock of the California Nurses' Association; Miss Goldman of the California Medical Assistants Association; Mr. Gould of the American Medical Association; Mr. Layton of AMPAC; and Doctors Anderson, Besson, Clark, Davis, Farley, Gibbons, Hoffman, Kilroy, Rossiter, Steinberg, Turner, Warrens, Wayburn, Wood and others.

35. *Adjournment*

The meeting was adjourned on Saturday, 27 May, at 4:40 p.m.

ALBERT G. MILLER, M.D., *Chairman*
HELEN B. WEYRAUCH, M.D., *Secretary*

REFERRALS OF 1967 CMA HOUSE OF DELEGATES RESOLUTIONS (Approved by the CMA Council on 27 May 1967)

| <u>Resolution</u> | <u>Title</u> | <u>Referral</u> |
|-----------------------|------------------------------------------------------------------|------------------------------------------------------------------------------|
| No. 1-67 | Welfare Prescription Forms | Commission on Public Agencies |
| No. 2-67 | RVS Identities for Staff Supervision of Public Hospital Trainees | Council and AMA Delegation |
| No. 3-67 | Certification and Recertification | Commission on Hospital Affairs |
| No. 6-67 | Department of Rehabilitation Report—Fees | Commission on Medical Services |
| No. 7-67 | The Pasteurization of Market Milk | Legislative Committee |
| No. 8-67 | Physicians' Employees' Health Coverage by CPS-Blue Shield | CPS Board of Trustees Commission on Professional Welfare |
| No. 9-67 | Quality Care | Bureau of Research and Planning |
| No. 10-67 | Drivers and Safety Standards | Commission on Community Health Services |
| No. 11-67 & No. 17-67 | Officers' Compensation | Finance Committee |
| No. 13-67 | Conservation | Commission on Community Health Services AMA Delegation |
| No. 14-67 | Study of RVS to be Changed to a Nomenclature with Code Numbers | Commission on Medical Services for study |
| No. 16-67 | CPS Medical Advisors | CPS Board of Trustees |
| No. 18-67 | Authorship of Resolutions | Executive Director and Speaker of the House |
| No. 19-67 | Witness Fees | Committee on Legislation |
| No. 21-67 & No. 56-67 | Medicare/Medi-Cal Identification Cards | CPS Board of Trustees |
| No. 22-67 | Implementation of Title XIX | AMA Delegation |
| No. 24-67 | Extended Care Facility Admittance | AMA Delegation |
| No. 26-67 | Nurse-Midwife Training Program | Committee on Maternal Child Care; Commission on Allied Health Professions |
| No. 27-67 | Cooperation with CCHPA | Committee for Emergency Action |

| <u>Resolution</u> | <u>Title</u> | <u>Referral</u> | <u>Resolution</u> | <u>Title</u> | <u>Referral</u> |
|-----------------------------------|--------------------------------------------------------|----------------------------------------------------------------------------------------|----------------------------------------------|-------------------------------------------------------------------------------------|-----------------------------------------------------------------------|
| No. 28-67 | Solid Waste Disposal | Commission on Community Health Services; AMA Delegation | No. 48-67 | Crippled Children's Program | Council |
| No. 29-67 | Smoking and the AMA | AMA Delegation | No. 49-67 | Nursing Home Payments | Commission on Public Agencies |
| No. 30-67 | Delegates, Limitation of Continuous Terms | Committee on Organizational Review and Planning | No. 50-67 | Disclosure of Source of Funds | Bureau of Research and Planning |
| No. 31-67 | Extended Care Facility Certification | ad hoc Committee on Extended Care Facilities; Committee on Legislation | No. 51-67 | Town-Gown Liaison | Liaison Committee to Medical Schools |
| No. 33-67 | Proposed Forms for the Introduction of CMA Resolutions | Executive Director | No. 53-67 | Today's Health Guide | Commission on Community Health Services; Commission on Communications |
| No. 34-67 | Integration and the Nursing Curricula | Commission on Allied Health Professions; CMA Representative to Health Manpower Council | No. 54-67 | Protective Helmets for Motorcyclists | Commission on Community Health Services; Legislative Committee |
| No. 36-67; No. 88-67 & No. 102-67 | Weight Reduction | AMA Delegation | No. 55-67 | Use of Marijuana, LSD and Other Hallucinatory Drugs | Scientific Board |
| No. 37-67 | CMA Committee on Emergency Medical Care | Commission on Community Health Services | No. 58-67 | Relative Value Studies | Committee on Fees |
| No. 38-67 | Financing of the Emergency Medical Care System | Commission on Community Health Services | No. 60-67 | Coverage for Out-patient Diagnostic Procedures | Commission on Medical Services |
| No. 39-67 | Reporting of Battered Child | Committee on Legislation; Public Health League; AMA Delegation | No. 61-67 | Medical Supervision of Blood Banking During Unscheduled Emergency Blood Collections | Committee on Blood Banks; Commission on Public Agencies |
| No. 40-67 | Restrict Meeting Time to CMA Business | Speaker of House | No. 62-67; No. 83-67; No. 98-67 & No. 101-67 | Medicare Laboratory Regulations | Commission on Public Agencies; AMA Delegation |
| No. 41-67 | Chiropractors and Medi-Cal | Committee on Legislation | No. 63-67 | Health Manpower Guidelines | Commission on Allied Health Professions |
| No. 42-67 | Usual and Customary Fees in Workmen's Compensation | Industrial Medical Committee | No. 64-67 | Family Physicians Training | Scientific Board; Liaison Committee to Medical Schools |
| No. 43-67 | PKU Testing | Committee on Legislation | No. 65-67 | Medical Care Form Review | Commission on Medical Services |
| No. 44-67 | Utilization Study of Closed Panels | Bureau of Research and Planning | No. 66-67 | Reciprocity Certification | Board of Medical Examiners |
| No. 45-67 | Commendation of CPS | | No. 67-67 | Extended Care Facilities | ad hoc Committee on Extended Care Facilities |
| No. 46-67 | Medi-Cal Payments in Teaching Hospitals | Council | No. 69-67 | Physical Evaluation of Class I and II Drivers | Commission on Community Health Services |
| No. 47-67 | Ambulance and Emergency Training | Commission on Community Health Services | No. 70-67 | Recognition of an Outstanding Effort | Commission on Communications |
| | | | No. 71-67 | Medi-Cal Drug Formulary | Commission on Public Agencies |
| | | | No. 72-67 | Radiological Consultation | AMA Delegation |
| | | | No. 75-67 | Federal Subsidies | Council |

| <u>Resolution</u> | <u>Title</u> | <u>Referral</u> | <u>Resolution</u> | <u>Title</u> | <u>Referral</u> |
|-------------------|----------------------------------------------------------------------|--------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|------------------------------------------------------------------------------|
| No. 76-67 | Admission Procedures to General Hospitals | Commission on Hospital Affairs | No. 96-67 | Laboratory Notification | AMA Delegation |
| No. 77-67 | Practice, Attempt to Practice Without a License, a Felony | Committee on Legislation | No. 97-67 | Communicable Disease Reporting | Commission on Public Agencies |
| No. 78-67 | Procedure for District Withdrawal from County Medical Society | Speaker of House | No. 99-67 | CPS By-law Amendment | CPS Board of Trustees |
| No. 79-67 | Income Tax Deduction for Medical Care | Committee on Legislation | No. 100-67 | California Blue Shield Commendation | |
| No. 80-67 | Technique to Expedite Use of Direct Payment Procedure Under Medicare | Commission on Communications | No. 103-67 | George C. Griffith, M.D. | Commission on Communications |
| No. 81-67 | Health Insurance for Individuals Over 65 | Commission on Medical Services | No. 104-67 | Virus Laboratory Services | Commission on Public Agencies |
| No. 82-67 | Certification and Recertification | AMA Delegation | No. 105-67 | Comprehensive Health Planning | Commission on Public Agencies; Commission on Community Health Services |
| No. 84-67 | Direct Patient Billing | Commission on Communications; Committee on Legislation | No. 108-67 | Legislation-Influenced Change in the Practice of Medicine | Commission on Hospital Affairs; Commission on Communications; AMA Delegation |
| No. 85-67 | Direct Patient Billing | Commission on Communications | REFERRALS OF 1967 HOUSE OF DELEGATES REFERENCE COMMITTEE RECOMMENDATIONS (Approved by the CMA Council on 27 May 1967) | | |
| No. 86-67 | Inhalation Therapy | Scientific Board; AMA Delegation | | | |
| No. 90-67 | Hospital Accreditation Requirement | Commission on Hospital Affairs | Reference Committee No. 1 | | |
| No. 91-67 | Compulsory Generic Prescribing | AMA Delegation | <u>Subject</u> | <u>Referral</u> | |
| No. 92-67 | Vexatious Litigation | Liaison Committee with State Bar Association | "Strengthening Health Care for Californians" | | Council and Commission on Communications |
| No. 93-67 | California Physicians' Service Commendation | | Inclusion of Page Highlighting Scientific Information in CALIFORNIA MEDICINE | | Council and Editor |
| No. 94-67 | Public Health League | Commission on Communications | Procedures for Reference Committee No. 1 | | Speaker of House |
| No. 95-67 | Role of Medicine in Society | Commission on Communications | Reference Committee No. 2 | | |
| | | | <u>Subject</u> | <u>Referral</u> | |
| | | | Dissemination of Budget Information | | Finance Committee |
| | | | Review of CMA's Role in Financing Medical Libraries | | Finance Committee |

❧ In Memoriam ❧

LOWELL SIDNEY GOIN, M.D.

March 3, 1891-June 4, 1967

DOCTOR LOWELL GOIN, a past president of the CMA, who died 4 June 1967 was born in Charter Oaks, Iowa, 3 March 1891. His preliminary education was in local schools. He entered St. Louis University School of Medicine and graduated in 1911 at 20 years of age—too young to be granted an M.D. The year of waiting until he was 21 years old, he spent as an intern at the Jewish Hospital. He then entered the University of Frankfurt, Germany, where he did post-graduate work for two years.

Returning to the United States, he practiced for some time in West Virginia and Illinois before coming to Los Angeles in 1926. He entered partnership in the practice of roentgenology with Dr. John W. Crossan of Los Angeles and in addition to his private work he was chief radiologist for Queen of Angels Hospital for many years and clinical professor of radiology at the University of California, Los Angeles.

That he was very active in his specialty is attested by his membership in the American Roentgen Ray Society, the Radiological Society of North America, of which he was a past-president, and the American College of Radiology, whose gold medal for outstanding achievement he had been awarded and of which he once served as president. He was a member of Alpha Omega Alpha and of Alpha Kappa Kappa.

Dr. Goin not only served the CMA as president (1944) but was an extraordinarily graceful steward of parliamentary procedure as speaker of the House of Delegates (1937-1943). Keenly interested and well informed in medical economics, he became a member of the first board of trustees of California Physicians' Service and followed Ray Lyman Wilbur, M.D., as president of the organization. He was a delegate from the California Medical Association to the American Medical Association for many years.

Dr. Goin lost a son in aerial combat over Germany in World War II. His other son, John M. Goin, M.D., is practicing medicine. He had three sisters, four brothers and three grandchildren. Dr. Goin's wife, Lillian Steuber, well-known concert pianist, survives him. This marriage meant much to Lowell.

Lowell Goin was a man of great accomplishment. He was a linguist of extraordinary ability, a musician of some standing and a composer of note. His rapier-like mind made him a master of repartee. He excelled as a debater and few dared contest him. A few people disliked him, many loved him and all admired him for his keenness of mind, his remarkable memory and his straightforward answers, however unpopular, on problems of the day.

Fame is fleeting and today many of our great men of medicine in California are almost unknown to the present generation. Lowell Goin should be remembered as one who gave much to his profession and his country. There were giants in his day and he was one of them.

E. VINCENT ASKEY, M.D.

BULPITT, JOHN MUNCEY (J. MUNCEY), Santa Ana. Died 11 May 1967, aged 71. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1918. Licensed in California in 1918. Doctor Bulpitt was a retired member of the Orange County Medical Association and the California Medical Association, and an associate member of the American Medical Association.



CAMPBELL, HORACE GRAHAM, Lindsay. Died 5 July 1967, aged 73, of arteriosclerotic heart disease. Graduate of Northwestern University Medical School, Chicago, Illinois, 1921. Licensed in California in 1923. Doctor Campbell was a member of the Tulare County Medical Society.



DETWILER, NEWTON HOWARD, Willits. Died 9 June 1967, in Willits, aged 53, of injuries received in an automobile accident. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1941. Licensed in California in 1941. Doctor Detwiler was a member of the Los Angeles County Medical Association.



ENSIGN, JOHNETTE GERTRUDE, Los Angeles. Died 30 June 1967, in Los Angeles, aged 63, of cerebral vascular accident. Graduate of the University of California School of Medicine, Berkeley-San Francisco, 1931. Licensed in California in 1931. Doctor Ensign was a member of the Los Angeles County Medical Association.



GLEETEN, SCOTT DILLON, Monrovia. Died 25 May 1967, in Monrovia, aged 91. Graduate of the University of Buffalo School of Medicine, New York, 1898. Licensed in California in 1919. Doctor Gleeten was a member of the Los Angeles County Medical Association, a life member of the California Medical Association, and a member of the American Medical Association.



GOODMAN, Minerva, Stockton. Died 1 July 1967, in Stockton, aged 90. Graduate of the University of Minnesota Medical School, Minneapolis, 1902. Licensed in California in 1903. Doctor Goodman was a member of the San Joaquin County Medical Society, a life member of the California Medical Association, and a member of the American Medical Association.



HART, DEAN ELDON, Oakland. Died 5 July 1967, in Piedmont, aged 63, of coronary arteriosclerosis. Graduate of Northwestern University Medical School, Chicago, Illinois, 1932. Licensed in California in 1932. Doctor Hart was a member of the Alameda-Contra Costa Medical Association.



JOHNSON, GILMAN CHESTER, Los Angeles. Died 26 June 1967, in Flagstaff, Arizona, aged 61, of heart disease. Graduate of the College of Osteopathic Physicians and Surgeons, Los Angeles, 1945. Licensed in California in 1945. M.D. degree from California College of Medicine, 1962. Doctor Johnson was a member of the Los Angeles County Medical Association.

KAY, GUY LESLIE (G. LESLIE), Redding. Died 12 June 1967, in Palo Alto, aged 77. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1917. Licensed in California in 1917. Doctor Kay was a retired member of the Shasta-Trinity County Medical Society and the California Medical Association, and an associate member of the American Medical Association.



MCMANUS, FRANK PAUL, San Carlos. Died 14 June 1967, in San Mateo, aged 80. Graduate of Washington University School of Medicine, St. Louis, Missouri, 1911. Licensed in California in 1914. Doctor McManus was a retired member of the San Mateo County Medical Society and the California Medical Association, and an associate member of the American Medical Association.



MYERS, CHARLES VINCENT, Los Angeles. Died 21 June 1967, in Los Angeles, aged 35. Graduate of the University of Tennessee College of Medicine, Memphis, 1955. Licensed in California in 1956. Doctor Myers was a member of the Los Angeles County Medical Association.



PETERS, ROGER A., Berkeley. Died 3 July 1967, aged 73, of cerebral hemorrhage due to arteriosclerosis. Graduate of the College of Osteopathic Physicians and Surgeons, Los Angeles, 1922. Licensed in California in 1923. M.D. degree from California College of Medicine, 1962. Doctor Peters was a retired member of the Alameda-Contra Costa Medical Association and the California Medical Association, and an associate member of the American Medical Association.



RUDOLPH, JEROLD DAVID, Santa Fe Springs. Died 5 July 1967, in Whittier, aged 45, of heart disease. Graduate of the College of Osteopathic Physicians and Surgeons, Los Angeles, 1956. Licensed in California in 1957. M.D. degree from California College of Medicine, 1962. Doctor Rudolph was a member of the Los Angeles County Medical Association.



SAMBUCK, ANTON JAMES, Watsonville. Died 12 June 1967, in Santa Cruz, aged 72, of heart disease. Graduate

of the College of Physicians and Surgeons of San Francisco, 1918. Licensed in California in 1918. Doctor Sambuck was a member of the Santa Cruz County Medical Society.



SHIREY, CHARLES WESLEY, North Hollywood. Died 12 June 1967, in North Hollywood, aged 83, of coronary artery disease. Graduate of the University of Pittsburgh School of Medicine, Pennsylvania, 1912. Licensed in California in 1917. Doctor Shirey was a retired member of the Los Angeles County Medical Association and the California Medical Association, and an associate member of the American Medical Association.



SHUTES, MILTON H., Carmel. Died 24 June 1967, in Monterey, aged 83, of cerebrovascular thrombosis. Graduate of Northwestern University Medical School, Chicago, Illinois, 1908. Licensed in California in 1913. Doctor Shutes was a retired member of the Alameda-Contra Costa Medical Association and the California Medical Association, and an associate member of the American Medical Association.



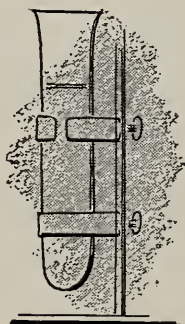
TUCKER, SIDNEY NATHANIEL, San Francisco. Died 2 July 1967, in Walnut Creek, aged 59, of acute myocardial infarction. Graduate of the University of California School of Medicine, Berkeley-San Francisco, 1935. Licensed in California in 1935. Doctor Tucker was a member of the San Francisco Medical Society.



WEYRAUCH, HENRY MARTIN, JR., San Francisco. Died 17 July 1967 in San Francisco of heart disease, aged 62. Graduate of Johns Hopkins University School of Medicine, Baltimore, 1929. Licensed in California in 1935. Doctor Weyrauch was a member of the San Francisco Medical Society.



WOOD, JAMES LESLIE, Oakland. Died 27 June 1967, in Berkeley, aged 58, of uremia. Graduate of St. Louis University School of Medicine, Missouri, 1937. Licensed in California in 1938. Doctor Wood was a member of the Alameda-Contra Costa Medical Association.



Planning and Goals Conference in Continuing Medical Education

Workshop Recommendations

Including Modifications Recommended by the Entire Conference and by the Scientific Board at Its Meeting, 1 April 1967

■ *Following are the recommendations drawn up by workshops held as a part of the Planning and Goals Conference in Continuing Medical Education, sponsored by the California Medical Association and directed by its Committee on Continuing Medical Education, San Diego, March 11-12, 1967. The conference was supported in part by Contract No. PH 108-67-158, Bureau of Health Manpower, Public Health Service, Department of Health, Education and Welfare.*

The general subject was divided among four workshops and the reports of two of them—No. 1, (a) and (b) and No. 2—are printed in this issue. The reports of the other two workshops will be published in succeeding issues.

The Role of the Community Hospital in Continuing Education

Report of Workshop 1 (a)

Discussion Leader—Phil R. Manning, M.D.

Secretary—Robert H. Quillinan, M.D.

I. *The need of the community hospital for education programs*

Because of the great changes that have come about in medicine, current methods of postgraduate education for the practicing physician have become inadequate. Many difficulties lie in the path of solving these inadequacies.

It is generally acknowledged that current medical school budgets and faculty are not adequate

to allow medical schools to assume significant direct teaching responsibilities to the practicing physician. It is felt that the time pressures on practicing physicians are such that many of them do not travel to medical centers. In addition, the "course approach" to continuing education is almost certainly not the most effective way for the physician to improve his skills and knowledge. The subcommittee, therefore, unanimously agrees that a major advance could be made if significant projects in continuing education could be introduced into the community hospitals.

II. *Existing programs in continuing education relating to the community hospital*

Most community hospitals already make certain attempts to allow their medical staff to educate themselves. For example, most hospitals have regular staff meetings and evaluate and report their mortality and morbidity statistics. Unfortunately, the majority of hospital staff meetings are prone

to be dull and uninteresting. The reports of mortality and morbidity statistics are often delivered in a routine way; and, frequently, these statistics are not utilized as a road map where improvements in medical care may be made.

Most community hospitals have a program committee whose duty it is to invite guest speakers to address the staff. However, very few community hospitals have organized committees which study problems of continuing education. Such a committee would be responsible for evaluation of problems in medical education. This committee would also be responsible for devising educational experiences that would aid the physicians in solving these problems. In short, the committee would be responsible for deciding what educational goals should be attacked and devising methods whereby these goals might be reached.

There are many avenues of continuing education that are already in existence. Frequently, a hospital staff is unaware of many of the educational opportunities. The CMA has taken the lead in notifying physicians of courses that are available. Some medical schools are also willing to render services in helping hospital staffs organize their local programs. The existence of these services is often not appreciated by the practicing community. The CMA could notify hospitals of services that might be available through the various medical schools.

Each year the California Medical Association sends out hospital survey teams. These survey teams often do not concern themselves with the continuing education that is going on within the various hospitals. It seems probable that considerable impetus to continuing education would be made if the survey teams would interest themselves in this problem.

III. Future development of continuing education in community hospitals

Inasmuch as there are no easy solutions to the problem of organizing continuing education within a community hospital, it seems logical that it will be necessary to explore various approaches. In many cases, projects could be tried out on an experimental basis. This would avoid the difficulty of hospitals being frozen into ineffective and inefficient projects. With proper control, experimental programs could be tested and the results shared with other hospitals. This would allow continued improvement in the approaches to continuing education.

It was the opinion of the subcommittee that the community hospital medical staff has an important role to play in its own continuing education within the community hospital.

Recommendations

I. It is suggested that the CMA encourage community hospital medical staffs to improve their self teaching by doing the following:

1. improve the academic aspects of hospital staff meetings;
2. obtain and make available self-instructional devices that may be utilized by individual staff members;
3. utilize mortality and morbidity statistics to give direction to future continuing educational programs within the hospital.

II. It is suggested that all community hospital medical staffs be encouraged to organize a committee to study problems of continuing education. This should not be confused with the regular program committee.

III. The CMA should communicate with hospitals to inform them of educational assistance that is available. For example, some hospital staffs do not know that some medical schools will help them with planning hospital staff meetings.

IV. It is suggested that the CMA hospital survey team examine the approach of each hospital staff to continuing medical education.

V. It is suggested that the CMA encourage community hospital medical staffs and medical schools to enter into experimental projects designed to discover feasible relationships that might be developed.

Personnel of Workshop 1(a)

Discussion Leader—Phil R. Manning, M.D., Los Angeles, Associate Dean, Postgraduate Medical Education, University of Southern California School of Medicine.

Secretary—Robert H. Quillinan, M.D., Sacramento, District Representative to the CMA Committee on Continuing Medical Education.

Participants:

Lewis T. Bullock, M.D., Los Angeles, CMA Councilor

David Covell, M.D., Pasadena, Associate Clinical Professor of Medicine, University of Southern California School of Medicine

James V. Dooley, M.D., Glendale, Associate Clinical Professor of Medicine, University of Southern California School of Medicine

Henry Dunlap, Los Angeles, Administrator, Children's Hospital

E. R. Evans, M.D., Long Beach, Medical Education Department, Memorial Hospital of Long Beach

Frank E. Hobden, Los Angeles, Director, Academic Communications Facility, University of California, Los Angeles, Center for the Health Sciences

Woodbury Perkins, M.D., San Diego, Director of Medical Education, Mercy Hospital.

John Peterson, M.D., Loma Linda, Professor of Medicine, Loma Linda University School of Medicine

Robert Randle, M.D., Pasadena, Director of Medical Education, Huntington Memorial Hospital

James Reavis, M.D., Bakersfield, Director, Medical Education, Kern County Hospital

Report of Workshop 1(b)

Seymour M. Farber, M.D., Discussion Leader

James C. MacLaggan, M.D., Secretary

THERE ARE VARIOUS DEFINITIONS of a community hospital and for purposes of simplification we are considering nonprofit hospitals, proprietary hospitals in most instances, Veterans Administration hospitals and a substantial number of county hospitals to be included in the broad group of community hospitals. University teaching hospitals, for purposes of discussion, are not considered as community hospitals.

Various subgroups were noted. County and Veterans Administration hospitals with teaching services and community hospitals with teaching services were differentiated from other community hospitals without teaching activities.

It was pointed out that the problems in each of these groups of hospitals varied greatly as did the methods of teaching the medical staffs of these hospitals.

It was strongly recommended that in any discussion of the role of community hospitals in continuing education, it is stated as the role of the community hospital *staff* in continuing education.

In recent years there has been a new development of importance in community hospital staff education, and that has been the appointment of part-time and full-time directors of medical education. It is noted that there is a national organization of the directors of medical education outlining their activities. Realistically, there is a great variation at the present time in the number of directors of medical education in hospitals and the types of duties assigned to them. In some instances part-time directors of medical education devote their

time to supervising the training of interns and residents. Others, on a full-time basis, organize medical activities and courses for the interns, residents and staff members.

Some hospitals, such as county hospitals, have full-time physicians in this area carrying out clinical duties as chiefs of specialty areas, such as surgery, medicine, etc.

Directors of medical education in hospitals expect that their duties will be broadened to encompass the continuing education of the practicing physicians of the staff. It was realized that their role has yet to be defined. Also to be defined is the type of men for this position, their training and background and skills. Until this definition comes about, it is expected that there will be a great variation in the type of men, their duties and how they are received in their activities by the staff members.

Who should pay the cost of postgraduate education? It was pointed out that in some hospitals with teaching staffs, this expense is legitimately added to the cost of care of the patient in the reimbursable formula of Title 18 of Public Law 89-97. In other areas insurance and other third-party payments for care of service patients is put in a fund for postgraduate education. Some hospitals depend on subsidies from pharmaceutical firms, others depend on voluntary health agencies. The consensus was that this cost should be borne by hospital staff dues or other staff controlled funds.

The role of the regional medical programs in financing and enlarging continuing education in community hospitals is one to be carefully evaluated. There are many encouraging factors in the regional medical program, but a cautionary statement was made, "if we want to be the piper, we have to be the payer."

It was felt that the motivating force to begin interest in postgraduate education should come through medical staff leadership within the hospital itself. It is realized that in many areas there is an excellent response in the community hospitals to continuing education, while in other areas substantial stimulation is highly essential to bring about approved programs. Methods of reaching the county medical society educational committees were discussed, and this included presentations by officers of the CMA regarding the importance of continuing education, help from field staff members of the CMA, the Medical Executives Conference, etc. It is hoped that by utilization of all high-level, as well as day-by-day practical approaches,

community hospital staffs will be activated in developing programs in continuing education.

It was pointed out that there are three areas in continuing education for the community hospital medical staffs to evaluate. The first is the *source of teaching*, and at the present time this is largely from medical centers. It is hoped that local physicians with teaching abilities would be included in these postgraduate efforts.

The second factor is the *transportation of information* concerning continuing education. In this area is the needed development of active programs in continuing education in hospitals now lacking this program. Information concerning this and stimulation for it can come from the CMA, the county medical societies, etc.

The third is the *recipient*—the physician who will be participating in continuing education. It was urged that the practicing physician not sit back and have things done for him. The stimulation of participation is an active learning process. It was again pointed out that continuing education is an evolutionary process and the practicing physician must be aware of the changes in himself as well as in teaching techniques.

A recommendation was made, for example, of the dialogue that can be developed by the pathologist and the physician at the time of the autopsy, with the inclusion of this dialogue as a part of the formal record on the chart of the patient.

The medical staffs of community hospitals have a unique opportunity through participating in continuing education mirrored in greater help for their patients, as well as having a rewarding experience. Continuing education of the medical staffs of community hospitals can best be experienced in day-by-day learning processes through a variety of methodology.

Personnel of Workshop 1(b)

Discussion Leader—Seymour M. Farber, M.D., San Francisco, Dean of Educational Services and Director of Continuing Education, Health Sciences, University of California, San Francisco Medical Center

Secretary—James C. MacLaggan, M.D., San Diego, President, California Medical Association

Participants:

J. David Bernard, M.D., Stockton, Director of Medical Education, San Joaquin General Hospital

Charles M. Blumenfeld, M.D., Sacramento, Member of CMA Committee on Maternal and Child Care

Nemat Borhani, M.D., Berkeley, State Department of Public Health; Coordinator, California Committee on Regional Medical Programs

Gordon Cumming, Sacramento, President-Elect, California Hospital Association

Gerald Escovitz, M.D., Arlington, Va., Acting Asst. Chief, Continuing Education Branch, Division of Physician Manpower, Bureau of Health Manpower, USPHS, HEW

Thomas A. Gonda, M.D., Palo Alto, Associate Dean, Stanford University School of Medicine

John G. Morrison, M.D., San Leandro, President-Elect, California Medical Association

David H. Payne, M.D., Long Beach, Medical Director, Pacific Hospital of Long Beach

Harry E. Peters, Jr., M.D., Oakland, President, Northern California Chapter, American College of Surgeons

Victor Richards, M.D., San Francisco, Member, CMA Scientific Board; Chief of Surgery, Presbyterian Medical Center

Pierre Salmon, M.D., San Mateo, Chairman, CMA Committee on Health Care of the Aged

Roger Shepherd, M.D., San Francisco, Assistant Program Director for Continuing Education, Presbyterian Medical Center

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Evaluation

Report of Workshop 2

Discussion Leader—Robert Tranquada, M.D.

Secretary—Harold I. Griffeath, M.D.

Panelists—Gerald Besson, M.D., and John Sheehy, M.D.

CHARGE: Arrive at recommendations for:

1. Suitable testing techniques for continuing education courses, as to their effectiveness;
2. How best to evaluate the quality of medical care in relation to continuing education of physicians.

The panel on evaluation claimed among its members a predictable assortment of practicing and academic physicians, as well as a welcome component of talent which included a systems engineer, the editor of *Audio-Digest*, a Past President of the Academy of General Practice, a member of the Board of Medical Examiners, and a television producer. This cross-section of talent and points of view resulted in a sometimes spirited and always representative exchange.

Initial discussion centered upon the first charge—that of arriving at recommendations “for suitable testing techniques for continuing education courses, as to their effectiveness.” It was agreed

that the word "effectiveness" required further definition. The consensus of the panel was that effectiveness should be measured with respect to the influence any given episode or system of continuing education might have upon changing the actions of a physician in the care of his patients.

This was recognized as a broad general goal, and it was agreed that the evaluation process would have to be applied more specifically to one or more of the following subcategories:

1. Knowledge and understanding
2. Skills and habits
3. Attitudes and values.

It was further agreed that these categories could not be divorced from their total influence upon the practice of the physician.

In an attempt to further categorize the areas in which effectiveness should be evaluated, it was concluded that the amount of information available to the panel would not allow further categorization. The primary reason for reaching this conclusion was the fact that we did not have a sufficient catalogue of the needs to which continuing education should respond.

At this point certain definite conclusions were reached by the panel in the form of the following recommendations to the conference.

- (1) It is of primary importance that we implement a procedure to identify those areas of Medical Care Practice which can be recognized as needing improvement by the following tests:
 - (a) High morbidity or mortality experience
 - (b) Expert opinion
 - (c) Informed public opinion

These areas should then be subjected to categorization according to the following considerations:

- (a) Those which are amenable to improvement with present educational techniques.
- (b) Those which will respond to educational techniques now available but not yet in use.
- (c) Those for which techniques are not yet available.

Additional consideration must be given to manpower availability to accomplish the necessary training, the time it would take to

bring about the change, and the potential economic gain by society.

- (a) It is recommended that such a project be undertaken with professional guidance, making use of systems analysis and of the advanced technologies now available in many areas of industry and science in addition to adequate use of medical consultation to provide appropriate direction.
 - (b) It is suggested that such a proposal be included in the suggestions offered to the California Committee for Regional Medical Programs, and that the potential benefits of such a program to industry might be used as an inducement for the contribution of talent and energy from that source.
- (2) Simultaneously, with the implementation of recommendation No. 1, it is recommended that we seek professional consultation to determine what are the presently available techniques for the evaluation of continuing medical education, and to place major emphasis upon the development of improved techniques with wider and more feasible applicability.
 - (3) It is recommended that we go beyond the measurement of simple cognitive gains to more complex measurement of changed physician performance in delivery of health care in an attempt to seek correlations which will eventually allow the use of simpler evaluation techniques.
 - (4) It is recommended that, if and when accreditation methods for continuing medical education are agreed upon, one of the prerequisites should be an adequate professionally directed system of evaluation of effectiveness with respect to the effect upon the practice habits of the physicians exposed to that experience.
 - (5) In view of the great importance to society of the development of effective continuing medical education and the central position of the medical schools in this field, it is recommended that appropriately qualified experts in the field of medical education should be active in

the continuing education departments of all medical schools to assist in the design, implementation and evaluation of the total educational effort.

Personnel of Workshop 2

Discussion Leader—Robert Tranquada, M.D., Los Angeles, Associate Professor of Medicine, University of Southern California School of Medicine

Secretary—Harold I. Griffeath, M.D., San Francisco, Chairman, CMA Committee on Cardiovascular Diseases; President-Elect, California Heart Association

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Gerald Besson, M.D., Sunnyvale, President, Santa Clara County Medical Society; Member, CMA Committee on Role of Medicine in Society; Assistant Clinical Professor of Medicine, Stanford University School of Medicine

Lois Lillick, Berkeley, Assistant Chief, Bureau of Chronic Diseases, State Department of Public Health

Vern Loudon, San Francisco, Producer, Director, Health Sciences Television Network, Continuing Education in Health Sciences, University of California, San Francisco Medical Center

Sarah Mazelis, San Francisco, Consultant in Education, Presbyterian Medical Center

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Herman Rannels, M.D., Orange, Medical Director, Orange County Medical Center

Steven Ross, M.D., San Francisco, Associate Clinical Professor of Radiology, University of California, San Francisco, School of Medicine

John Sheehy, M.D., Riverside, Member, CMA Advisory Committee on Quality of Medical Care Study; Member, CMA Bureau of Research and Planning

Justin J. Stein, M.D., Los Angeles, Member, CMA Scientific Board; Member, Board of Medical Examiners, State of California; Professor of Radiology, and Chief, Radiation Therapy Division, University of California, Los Angeles, School of Medicine

Lorin Stephens, M.D., Los Angeles, Assistant Clinical Professor of Orthopedic Surgery, University of Southern California School of Medicine

Thomas Weber, Ph.D., Fullerton, Advanced Research, Advanced Technology Operations, Beckman Instruments, Inc.

George J. Wittenstein, M.D., Santa Barbara, Chairman, Committee on Continuing Education, Santa Barbara County Medical Society; Clinical Instructor, Surgery, University of California, Los Angeles, School of Medicine



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Organizing for Health Care

A Report by the Committee on the Role of Medicine in Society
California Medical Association

THE PUBLIC EXPECTATION for high quality health care at a reasonable overall cost for every person who needs it will somehow be satisfied. This desire is for "mainstream" comprehensive personal medical care which will utilize a broad range of community health services wherever they may be required in prevention, diagnosis, treatment or rehabilitation. It appears likely that on-going change and organizational innovation will be needed if these expectations are to be fulfilled. The Committee on the Role of Medicine in Society believes that medicine as a whole and CMA in particular now have an important responsibility to encourage study and experiment and to assume leadership with action programs in organizing for ever better health care.

Why More Organization Is Needed

The fundamental reality which underlies the need for more attention to the organization of health care is both simple and compelling. It is the fact of scientific and technologic progress and the inescapable impact these have had and will continue to have upon both medicine and the society it serves. As science proliferates so does specialization. This specialization has occurred not only among the academic disciplines and in their technologic application but also in medical practice and in society itself, where an ever increasing number of functions are becoming specialized. The corpus of health care has now come to embrace many

highly differentiated functions, and also structures, which must somehow work smoothly and efficiently together if the goals of high quality health care at a reasonable cost are to be achieved. The specialized elements of any complex organization are necessarily interrelated, and while they may have a desirable degree of autonomy and independence, nevertheless in a very real sense they are interdependent. If the overall task is to be accomplished effectively and efficiently they must work together with some sort of ground rules and within some sort of operational framework. The need to accomplish this for health care, to the satisfaction of the public expectations, now challenges the well-known American genius for voluntary organization.

National Concern with Organization in Health Care

National concern with organization in health care is not new. The recommendations of the Committee on Costs of Medical Care (Wilbur Committee) published in 1932 dealt with organization in health care in a broad sense. An earlier report of the CMA Committee on the Role of Medicine in Society, "Prologue and Perspective," indicated that much has happened over the years which might be interpreted as implementing the recommendations of the Committee on Costs of Medical Care (Wilbur Committee). Yet, even the massive efforts of professional schools, professional societies, hospital professional staffs, voluntary health agencies, and the health care industry, many of which were influenced and motivated by the American Medical Association, have fallen short of the present public expectations. There are expressions of dissatisfaction with research which some in government say should be more health need oriented, with education which has not been able to meet present manpower requirements, and with patient care which allegedly has not sufficiently empha-

This is the third of three articles by the Committee on the Role of Medicine in Society that have been received by the Council and the House of Delegates of the California Medical Association. No official action has been taken on them by either body and they are being published here as they were received by the Council and the House of Delegates, for information.

The first article, "Responsibility for Quality in Health Care," was printed in the June 1967 issue of CALIFORNIA MEDICINE, and the second, "A New Relationship with Government and Others," was published in the July issue.

Committee on Role of Medicine in Society: Gerald Besson, Burt L. Davis, Sanford Feldman, Elmer F. Goel, Malcolm C. Todd, and Malcolm S. M. Watts, chairman; and ex officio Samuel R. Sherman and Ralph C. Teall.

Reprint requests to: California Medical Association, 693 Sutter Street, San Francisco 94102.

sized prevention and health maintenance, nor reflected new knowledge in every-day practice with sufficient promptness, nor succeeded in realizing the social goal of a high quality of comprehensive care equally accessible to all.

In recognition of this problem the National Health Council and the American Public Health Association, both voluntary non-profit associations, joined together to create a non-governmental National Commission on Community Health Services. This Commission has carried out various surveys, studies and workshops over a period of several years and has recently published its report "Health Is a Community Affair." This report addresses itself to many aspects of organizing for health care and makes many recommendations. The report is briefly surveyed below.

"Health Is a Community Affair"

The Committee on the Role of Medicine in Society believes the report "Health Is a Community Affair" of the National Commission on Community Health Services deserves careful examination. It is founded on a broadly based study and many of its recommendations are certain to have substantial support in both government and voluntary circles.

The Commission formulated 14 positions or "statements of conviction" and approximately 100 specific recommendations. The position statements covered the subject areas of:

Health Services and Jurisdictional Areas

Comprehensive Personal Health Services

The Changing Role of the Personal Physician

Comprehensive Environmental Health Services

Control of Man's Environment

Accident Prevention

Family Planning

Urban Design and Health

Education for Health

Health Manpower

Hospital Care

Organization, Administration, and Financing of

Official State and Local Health Agencies

Voluntary Citizen Participation

Action-Planning for Community Health Services

The following are some of the more significant excerpts underlying each of the subject areas to which the Commission addressed itself:

Health Services and Jurisdictional Areas

"Health service administrative areas must be efficiently functional in terms of major health problems and can no longer be circumscribed by traditional community, state, and national boundaries.

"The organization and delivery of community health services by both official and voluntary agencies must be based on the 'community of solution' . . ."

Comprehensive Personal Health Services

"All communities of this nation must take the action necessary to provide comprehensive personal health services of high quality to all people in each community. These services should embrace those directed toward promotion of positive good health, application of established preventive measures, early detection of disease, prompt and effective treatment, and physical, social and vocational rehabilitation of those with residual disabilities.

"It will require the removal of racial, economic, organizational, residence, and geographic barriers to the use of health services by all persons. It will require strengthened and expanded licensure and accreditation of services, manpower, and facilities. It will require maximum coverage through health insurance and other prepayment plans, and extension of such insurance to cover the broad range of services both in and out of hospitals. Finally, success will require a citizenry that is sufficiently well informed and motivated to follow established principles conducive to good health, and to cooperate fully with health services in all phases of prevention and treatment of illness and disability."

The Changing Role of the Personal Physician

"Every individual should have a personal physician who is the central point for integration and continuity of all medical and medically related services to his patient. Such a physician will emphasize the practice of preventive medicine, both through his own efforts and in partnership with the local health and social resources of the community. He will be aware of the many and varied social, emotional, and environmental factors that influence the health of his patient and his patient's family. He will either render, or direct the patient to, whatever services best suit his needs. His concern will be for the patient as a whole and his relationship with the patient must be a continuing one."

Comprehensive Environmental Health Services

"Optimum health can be fostered by prospective planning and management of comprehensive environmental health services."

Control of Man's Environment

"Improving the quality of our environment requires additional financial resources, public and private, adequately planned and programmed to insure the control of water and air pollution and protective measures against contamination from physical, biological, and chemical products, including the increasing use of radioactive materials."

Accident Prevention

"Accident prevention is an integral part of comprehensive personal and environmental health services. Health leadership must increase its efforts to prevent accidental injuries, disabilities, and death."

Family Planning

"Family planning should be an integral part of community health services. Private and public health agencies must accept responsibility for provision of family planning services and for the support of scientific research on human fertility. Family planning is essential to individual and family health and contributes to a healthy community."

Urban Design and Health

"Planning for a health environment is an essential consideration in urban design. Immediate steps must be taken by those responsible for the control of land use, transportation, economic development, and related physical and social planning to coordinate their activities to provide for the most effective use of space for our rapidly growing urban population densities; reduce hazards to physical and emotional health from overcrowding where it exists; and contribute to an aesthetically and emotionally satisfying environment conducive to positive health."

Education for Health

"Education for health is a fundamental aspect of community health services and is basic to every health program. It should stimulate each individual to assume responsibility for maintaining personal health throughout life and to participate in community health activities."

Health Manpower

"Every community must have available the skills and techniques of many kinds of health personnel. These needs are increasing in terms of numbers of people as well as kinds of skills required. The wide range of manpower for environmental and personal health services includes not only engineers and physicians, but many varieties of laboratory technicians, dentists, nurses, pharmacists, physical, occupational, and speech therapists, homemakers, health aides, social workers, psychological and vocational counselors, and nutritionists."

"To deliver comprehensive health care, all members of the health team must work together, with each member consistently contributing his most highly developed skills and recognizing others' skills and particular contribution to the health of people. They must, at a minimum, coordinate their work."

Hospital Care

"The rapid rise in the cost of hospital care in the past two decades is a matter of grave concern to the American people. The upward pressure on costs results from the development of new and costlier diagnostic and treatment techniques; increases in salary costs as hospital wages become competitive with industry; the increasing burden of educational and training programs in hospitals; and the inability of hospitals to match rising costs with increased productivity."

". . . further increases in hospital costs must not be accepted complacently, but that a wide range of vigorous and persistent actions must be taken by all parties concerned to moderate the costs of hospital care without adverse effects on its quality."

Organization, Administration, and Financing of Official State and Local Health Agencies

"Every state should have a single, strong, well-financed, professionally staffed, official health agency with sufficient authority and funds to carry out its responsibilities. The state should assure every community of coverage by an official health agency and access to the complete range of community health services."

"This single agency, in which all the major health programs of the state government should be concentrated, would be able to coordinate the various environmental, preventive, curative, and rehabilitative components into a comprehensive

health service system. It should be responsible for setting the health standards of other state programs even though they may be a secondary activity of another agency."

Voluntary Citizen Participation

"Government, private business, and voluntary associations all contribute to the health system. Public and private elements are mutually interdependent. The work of government and voluntary organizations is particularly enhanced by the degree of voluntary citizen participation involved in their processes and services.

"The extension of this tradition of voluntary citizen participation will be essential in guiding the development of community health efforts and in providing important elements of service."

Action-Planning for Community Health Services

"The nature of today's society and the complexities of health and other community services require a broad approach to planning and action which can be fitted to each particular community situation, yet is in harmony with broader trends and is capable of further development and change . . . planning is an action process and is basic to development and maintenance of quality community health services. Action-planning for health should be community-wide in area, continuous in nature, comprehensive in scope, all-inclusive in design, coordinative in function, and adequately staffed.

"Health service objectives can be met through processes which provide opportunity for citizens to work together to understand, identify, and resolve problems, to set intermediate and long-range goals, and to act to achieve the goals."

Comprehensive Health Planning Act (PL 89-749)

In the final days of the 89th Congress PL 89-749 was enacted. This law creates what has been called an "intergovernmental partnership for health" by strengthening the linkages among federal, state and local governmental health agencies and by regrouping many U.S.P.H.S. grants so as better to meet priorities to be determined by states and communities. The law will establish a continuing process of comprehensive health planning at the state and regional levels and will support local and regional planning by governmental and non-governmental bodies on a continuing basis. Depending on how the various provisions of this

act are interpreted or administered, its operation can have a profound effect on almost all facets of health care. PL 89-749 actually provides a legislative framework within which many of the recommendations of the National Commission on Community Health Services can be carried through to fruition.

Some "Inevitables for Medicine"

The Committee on the Role of Medicine in Society believes that if medicine is to play its most constructive role in planning and organizing for ever better health care, certain "inevitables" (to borrow Ward Darley's concept) should be recognized.

*"Inevitables" in Medicine**

- Increasing knowledge.
- Increasing specialism.
- Increasing demands for service.
- Increasing costs of service (particularly the total national expenditure).
- Increasing shortages of personnel (relative to demand).
- Increasing complexity and efficiency in data processing and communication.
- Increasing institutionalization (organization for the delivery of health care).

To the foregoing, the Committee would add:

"Inevitables" in Society

- Increasing mobility of doctors, nurses, other health care personnel, patients and problems.
- Increasing expectations for better health in the World Health Organization definition, "a state of complete physical, mental and social well-being and not merely the absence of disease."
- Increasing automation of many aspects of health care.

"Inevitables" in Relations Between Medicine and Society

- Increasing complexity in every aspect of providing high quality health care.
- Increasing interaction between medicine and society with increasing involvement at many levels.
- Increasing need for foresight, planning, decision and action oriented programs.

*Darley, Ward, M.D.: "American Medicine and the Inevitables in Its Future," *Journal of the American Medical Association*, 18 April 1966, Vol. 196, No. 3, p. 177.

- Increasing need to carry on an ever growing number of activities simultaneously and in a co-ordinated manner.

Objective and Opportunity

The overall objective of medicine has always been the best possible health care for the individual who needs it. This objective has been and continues to be sound. Within this overall objective medicine has always felt that voluntary systems are preferable to compulsory systems, that problems of health care are generally better solved on the local than at the national level, and that financial involvement by government in any aspect of health care carries with it the danger that this involvement may lead eventually to entanglement in a morass of federal bureaucracy and ultimate federal administrative control.

It is suggested that this overall objective of medicine is as valid now as it ever was. Perhaps, paradoxically, the thrust of much of the recent federal health care legislation and the invitation to "partnership with government" carries with it a heavy emphasis on local initiative, voluntary organization and local or regional control. This now presents medicine with an unusual challenge and an increased opportunity for constructive and organized activity to forward its long standing overall objective.

The Committee on the Role of Medicine in Society believes that medicine, and the CMA, should play a vital and responsible role. It is quite obvious that neither government nor any other body can force voluntary initiative or leadership to come into being. This would be a contradiction in terms. It is equally obvious that government has the power to act if voluntary leadership does not appear or does not meet the public expectation. "Health is a Community Affair" may become "health is a government affair" in the absence of effective voluntary action.

Some Suggestions for Action

The Committee on the Role of Medicine in Society believes that medicine and the CMA may now identify six specific areas where there is a particular need for determined action to organize a prompt and effective contribution by medicine to the overall team approach to health care. Each is discussed briefly in this report.

Professional Organization

The Committee would like to give some expression to the feelings of many that a professional

organization designed over a hundred years ago may now need some fundamental change or adaptation of both form and function if it is to perform with maximum effect in the new health care environment. For example, many people suggest that the part-time and generally temporary leaders who are elected to office in associations of physicians may all too often be disadvantaged by their contemporary full-time and more or less permanent leaders in insurance, labor, management, government and elsewhere. Medical associations appear to be too "resolution oriented" in an "action oriented" environment. There is fractionation, and it is not certain that the organizational patterns reflect the interests and aims of the members as directly as might be. There is little organizational provision for more formal links with other groups and organizations which share responsibilities in health care, although CMA has led notably in this. Organizational foresight, research, communication and decision making are too often hard to come by and too apt to fall short of what is really required in the complex, rapidly changing situations of the modern environment.

Quite obviously, if organized medicine is to play a leading role in organizing for health care, its own organizational instrument must be shaped and sharpened to deliver the most effective kind of performance. The CMA has wisely created a Committee on Organizational Review and Planning and has assigned to it the responsibility to examine the organizational structure of CMA to determine if and how this might be better adapted to the responsibilities of organized medicine in the present environment. This report will therefore not concern itself with this important task which is so central to the effectiveness of the CMA, and perhaps of medicine as a whole.

The "Health Team"—Health Manpower

The phrase "health team" is enjoying increasing use as a term to encompass what is involved, but as yet "health team" has little or no definition. At the very minimum its elements include the physician, the patient and the allied health professions. Others would add the academic health scientists as well as the host of technicians and other professionals who comprise what is loosely called the "health care industry." In this sense the terms "health manpower" and "health team" become almost synonymous. No matter what the definition, it would seem that the realities of growing spe-

cialization and growing interdependence among specialists will require some organizing of the "health team."

A number of problems are sure to loom upon the horizon. It would seem that some kind of generic or overall health team framework will be needed which will reflect and formalize the broad functions of each of the various segments. Understandings will be necessary among all concerned with respect to who is responsible for what. Working agreements will be required in many broad areas of professional status, personnel qualifications, instruction and training, as well as responsibility in patient care, if the total operation is to be smooth, efficient and economical. There must be acceptable and approved criteria of quality for the health team as a whole as well as of its parts. There must be acceptable ethics. There will be problems of career satisfaction, career fulfillment and adequate compensation for all members of the "health team." The Committee agrees with the report "Health is a Community Affair" which affirms the central role of the "personal physician" on this health team.

There surely is an important opportunity for imagination and leadership in the development of the specifics of these concepts. The Committee believes that the CMA should address itself to what is involved and assume leadership with others in organizing a health team framework which will relate the broad functions of the various segments to one another, including personnel qualifications, instructional and training requirements and delineation of responsibility in patient care, and at the same time encourage the development and use of more or less temporary teams within this overall framework.

Community and Regional Health Services

The Committee believes that more attention to organizing community and regional health services is both a necessary and an inevitable result of scientific progress, and increasing public expectations in health care. The Committee further believes that as this organizing occurs there should be strengthened the concept of a personal physician for every person and with it "personalization" of the medical care which is to be equally accessible to all. The aim should be simultaneously to improve the organization and also the individualization of health care, and to retain as much local initiative, supervision and control as possible.

The personal physician concept is one long espoused by CMA and is now endorsed as a prominent feature of the National Commission on Community Health Services report. The *Second Progress Report* of the Committee on the Role of Medicine in Society drew attention to a very real need to emphasize personalization in medical care at this moment in history when rapid scientific progress and specialization often seems about to overwhelm the dignity and individuality of persons. The enactment of the "Comprehensive Health Planning and Public Health Services Amendments of 1966" (PL 89-749) called by some the "Partnership for Health Bill" focuses new governmental attention and also funds upon planning for health services. While this law places the primary responsibility with the state departments of health, which will establish health planning agencies for the purpose, provision is also made for comprehensive health planning by local public or non-profit private agencies on a regional, metropolitan or other local basis. This would provide needed funding for local planning under the aegis of the private sector. There are already many communities with local or area wide social planning or health councils which vary in their vision and effectiveness. Health facilities planning by government supported voluntary agencies is being tried in several parts of the state. A number of component medical societies of the CMA have planning committees of one sort or another. The Committee believes that these activities should be encouraged and expanded by CMA. In general, however, it seems fair to say that in most communities the planning effort has somewhat lagged behind the planning need.

The Committee believes that the present situation offers a major opportunity for medicine, the CMA and its component societies to play a central role, joining with others who share responsibility for health care, in organizing community and regional health services at the local level. These efforts can place appropriate emphasis on the personal physician and the personalization of health care. It should be recognized that this will involve both an understanding and a personal effort on the part of every practicing physician as well as by the local physician leadership. The Committee suggests that "Community Action for Personal and Community Health" become an action program of CMA, its component societies, and its members; and that CMA should undertake to develop an outline and material for such

an action program, perhaps in collaboration with those component societies which have had some interest and experience in this field.

Regional Medical Programs

The "Heart, Cancer and Stroke Amendments of 1965" (PL 89-239) have the following purposes:

- To encourage and assist, through grants, in the establishment of regional cooperative arrangements among the medical schools, research institutions, and hospitals for research and training (including continuing education) and for related demonstrations of patient care in the fields of heart disease, cancer, stroke, and related diseases.
- To afford the medical profession and medical institutions, through cooperative arrangements, the opportunity of making available to their patients the latest advances in the diagnosis and treatment of these diseases.
- To improve the health manpower and facilities available to the nation without interfering with the patterns or methods of financing of patient care or professional practice or with the administration of hospitals and in cooperation with practicing physicians, medical center officials, hospital administrators, and representatives of voluntary health agencies.

This law envisions that regional medical programs will be developed in conjunction with local advisory groups which it states must include "practicing physicians, medical center officials, hospital administrators, representatives from appropriate medical societies, voluntary health agencies, and representatives of other organizations, institutions and agencies concerned with activities of the kind to be carried on under the program and members of the public familiar with the need for the services provided under the program." The thrust is that the programs are to be generated and controlled on a local and regional level and that there must be active participation by a broadly based group. The programs themselves are to have the primary aim of promoting the use of new knowledge and new techniques in day-to-day patient care.

The CMA has joined with others to create a California Committee on Regional Medical Programs, and the California Medical Education and Research Foundation has been given a planning grant which will enable the C.C.R.M.P. to stimu-

late the development of these programs in California.

The Committee believes that the regional medical programs could become a most valuable aid to the betterment of health care in California and supports the principles of local initiative, local autonomy and local control embodied in the law. It suggests that much will depend upon whether these principles can be made to work effectively so that suitable programs will come into being and so that gaps and overlaps will be avoided. The Committee suggests that CMA and its component societies promptly undertake an organizing role at the level of the local and regional advisory groups in order that full advantage may be taken of the opportunity to accomplish the intent and purposes of the law as enacted, at both local and regional levels throughout the state. A specific action program, coordinated by CMA, is suggested to accomplish this.

Organizing for Health Care at the State Level

It is quite apparent that for a number of reasons many important functions of planning and organizing for health care will be carried on at the state level. California is fortunate to have a tradition of communication and cooperation among the CMA, the California Hospital Association, the Board of Medical Examiners and the various branches of State government concerned with one or another aspect of health care. This includes the Health and Welfare Agency in particular, and the Departments of Public Health, Mental Hygiene, Social Welfare, Rehabilitation, Finance as well as other agencies of State government. CMA participation has been creative and has produced important results. These efforts have earned respect for CMA and its leaders not only in California but throughout the nation. CMA has also participated in numerous voluntary efforts with numerous voluntary agencies as well as contributing to the whole through the activities of its several non-profit subsidiaries. This record of achievement forms a solid basis for an effective CMA role in helping to organize for health care at the state level.

The Committee believes that planning, cooperation and coordination among public and private agencies and organizations at the state level will become increasingly important. This is underscored by the additional responsibility which the "Comprehensive Health Planning and Public Services Amendments of 1966" (PL 89-749) gives to

the health planning agencies in state departments of public health. If there is to be truly a pluralistic approach the government sector and the private sector each must contribute its full share of effort and know how, with full recognition given not only to the autonomy and independence of each of the participants but also to their separate responsibility to do their full share.

The Committee suggests that the CMA at this time should strengthen and build upon the foundation of its close and successful relationships with statewide organizations and agencies. The efforts to work with the public sector to improve governmental health care programs have been productive and should be continued. However, the Committee also suggests that medicine and CMA recognize and accept a larger role in the private sector. It is curious to note how much more time and effort organized medicine has spent attempting to improve government programs than it has in trying to strengthen and perfect the private sector. This imbalance should now be corrected and action programs should be developed promptly to stimulate leadership, understanding, organization and effectiveness in the private sector, so that it can become an increasingly vital force in organizing for health care at the state level and fully able to do its share in helping to meet the expectations of the public.

A National Academy of Health

It is quite clear that the American Medical Association does not embrace all of the important non-governmental interests which are essential to medical care and health, nor is there any clear focus of leadership or direction in the private sector at the national level. The Congress and the Federal administration tend to turn to the United States Public Health Service, or to the Association of American Medical Colleges, the American Public Health Association, the American Hospital Association, to the specialty societies, to such organizations as the Physicians Forum or the Group Health Association, or to specially constituted bodies such as the President's Commission on Heart Disease, Cancer and Stroke or the National Commission on Community Health Services for advice on matters of national medical policy, rather than to the AMA. This was not always so, and it is likely that the very strong political stand against compulsory hospitalization coverage under Social Security, taken for better

or worse by the AMA with the full support of a large majority of its membership, not only blocked effective communication between the Federal government and AMA for many years but also effectively closed the door to the possibility of AMA being regarded as an unimpeachable and unbiased advisor on the nation's health or on organizing for health care. This communication is now being reestablished and the doors of government are being reopened to the AMA and other physicians' organizations.

There is little doubt that health care, government, and politics will be intimately entwined for the foreseeable future. Clearly, organized medicine has knowledge, abilities and expertise to contribute to the development of health care in this nation. Donald K. Price, M.D., President-elect of the American Association for Advancement of Science, in speaking of science, has stated "our best hope is for a science which will grow not as a guild under the patronage of a traditional sovereignty, but as a most important element in a highly diversified free system. In this system the scientist gets his influence not from a complete detachment from politics but from sharing the political obligations of society."

The basis for the position of influence from which science speaks so effectively has as its foundation the National Academy of Sciences. The Congress and the other branches of government turn to this Academy for advice on matters of scientific policy. Although the Academy is established under a charter from the Congress, it is an elite self-perpetuating body of top scientists. No federal funds flow to the Academy for its support and its independence is unquestioned.

The Committee (along with others) suggests that perhaps the time has come to propose a "National Academy of Medicine" or a "National Academy of Health Care" to provide a comparable non-governmental framework in which the many interests in health care could exchange their thinking and experience, carry on appropriate study and investigation, and which could be authoritative and advisory not only to government but to all the participating interests in health care. The Committee believes that "organizing for health care" in the present-day environment requires that some such action as this be taken and suggests that CMA examine this and like proposals with a view to urging their adoption at the national level.

Recommendations

The following recommendations were drawn by the Committee on the Role of Medicine in Society from its reports, published serially in this and the two preceding issues of CALIFORNIA MEDICINE.

I

With regard to the "Responsibility for Quality in Health Care" [CALIFORNIA MEDICINE, June 1967, pages 486-490], the first part of a three-part report, the Committee on the Role of Medicine in Society recommends that:

- The California Medical Association assume the responsibility for attempting to develop an Index for the assessment of the quality of medical care and, if such proves to be feasible, to assume the responsibility for its appropriate application.
- The CMA assign this task to an appropriate Commission(s) or Committee(s) which may be augmented with such consultants as are needed.

II

From the second part of the report, "A New Relationship with Government and Others" [CALIFORNIA MEDICINE, July 1967, pages 109-114], the Committee drew the following recommendations:

The Committee recommends that:

1. The California Medical Association reaffirm its long established policy and continue its efforts to develop and maintain such cooperative arrangements as are needed to enhance teamwork in the interest of improving health care.

2. The California Medical Association reaffirm its recognition of the vital role of the Bureau of Research and Planning and encourage this unique information and fact-gathering arm of the medical profession to continue to develop that body of knowledge and expertise which organized medicine must somehow master if it is to make its most effective contribution to the advancement of health care in present-day society.

3. The California Medical Association continue, by precept and example, to encourage the medical profession to involve physicians and their organizations in all phases of organizational planning and activity in which the health care of the public is concerned.

4. The California Medical Association and the California Medical Education and Research Foun-

dation actively seek appropriate funding from private or public sources which will enable the medical profession to engage in a greater variety of research, educational and service activities which will benefit the public and health care.

5. The California Medical Association, by precept and example, encourage the medical profession to intensify its efforts and assume a primary responsibility to create an environment of better public understanding of high quality health care and of greater public support of the medical professions' ideals, goals and involvement in the provision, surveillance and financing of this high quality health care.

6. The California Medical Association, in dialogue and in action, stand firmly upon the principles (a) that the physician and the medical profession are knowledgeable concerning what is involved in individual health care, (b) that individuality and personal dignity are important in health care and this will always require a plurality of solutions in medical care, (c) that adequate financing from whatever source is essential if high quality health care is to be rendered, and (d) that the public should be kept accurately and currently informed of progress or lack of progress toward the common goal of making a high quality of health care available for every citizen.

III

From part three of its report, "Organizing for Health Care" [in this issue of CALIFORNIA MEDICINE], the Committee recommends that:

1. The California Medical Association recognize that there are complex problems with respect to the training, responsibilities and effective utilization of the allied health professions within the framework of present-day health care, and that it assign to an appropriate committee the responsibility, in collaboration with others, for identifying and delineating the components and responsibilities of the "health team" as well as recommending their relationships to physicians in all types and specialties of practice.

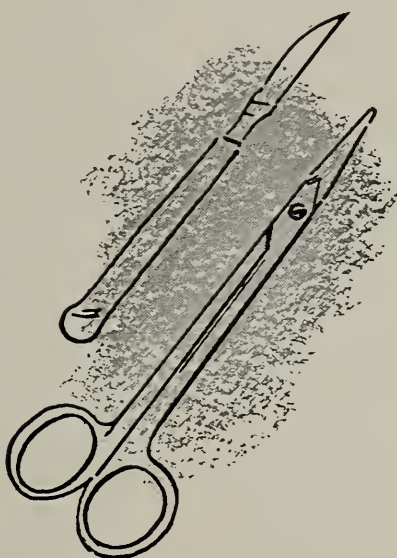
2. The California Medical Association, its commissions and committees and its constituent societies study "Health is a Community Affair" (a recent report of the National Commission on Community Health Services) and the "Comprehensive Health Planning and Public Health Services Amendments of 1966" (PL 89-749), and that an appropriate committee of the CMA be charged with evaluating these studies and their recommendations, and with developing an action program for CMA and its component societies which will emphasize local planning and coordination, under the aegis of the private sector, and also give substance to the central role of the personal physician in any community or regional organization of health care service which might develop.

3. The California Medical Association continue its interest in and support of the California Committee on Regional Medical Programs, and that an appropriate committee of the CMA be charged with the responsibility of developing suggestions for action programs to enable the CMA and its constituent societies to play a useful and

important role in helping to create local and regional programs which will implement the present and worthwhile purposes of the "Heart, Cancer and Stroke Amendments of 1965" (PL 89-239).

4. The California Medical Association continue its long-established and productive liaison with other statewide public and voluntary organizations concerned with health care, and that this participation now be extended, particularly in the private and voluntary sectors, where planning, cooperation and coordination can and should be significantly strengthened at this time.

5. The California Medical Association encourage a study of the desirability of creating a National Academy of Medicine (or Health Care), on the general model of the National Academy of Sciences, which with representation from all the health care professions could serve as their spokesman in matters relating to the scientific and sociologic aspects of health care and advise government on the formulation of public policy as it relates to health care.



PUBLIC HEALTH REPORT

Lester Breslow, M.D., M.P.H.
Director, State Department of Public Health

AT THE SUGGESTION of the CMA's Committee on Public Health, the following resume of California's premarital examination law and procedures the physician should follow has been prepared.

Questions are not infrequently asked by physicians concerning the extent of medical examination necessary to meet the requirements of the premarital examination law.

In performing the examination the physician should question the applicant concerning previous signs, symptoms or therapy for syphilis and should perform a physical examination in addition to the blood test.* It is the intent of the law that each applicant have a physical examination sufficient to determine the presence or absence of infectious syphilis. A blood serologic test alone does not satisfy this requirement.

The minimal physical examination procedure for the purpose of determining the presence or absence of infectious syphilis should include visual examination of the entire skin (including the palmar and plantar surfaces), the mucous membranes and the mucocutaneous junctions, particularly the oral, genital and rectal areas. Without such examination, it is doubtful that communicable primary and secondary syphilis could be properly diagnosed, particularly seronegative primary syphilis. Conversely, reaction on serologic test does not necessarily indicate infectious syphilis. If the physician is assured that a patient with syphilis has had adequate treatment and is no longer infectious, it is appropriate to sign the premarital examination certificate.

Under the law, the examination and serologic test must be made within 30 days preceding the issuance of the marriage license, and all certificates and reports must be kept confidential.

*In California last year 284,917 persons had premarital examinations, compared with 283,576 in 1965. Of the serologic tests for syphilis in connection with these examinations, 0.93 per cent were reactive in 1966 and 1.01 per cent in 1965.

It is, of course, advisable in connection with the premarital examination to be sure the candidates are free of gonorrhea or other venereal or communicable diseases. Although the marriage health certificate may not be withheld on account of the presence of gonorrhea, California law prohibits willful exposure of another person.

Premarital examination procedures for the physician are as follows:

1. Conduct a physical examination.
2. Submit a specimen of blood to an approved laboratory. This may be the laboratory which regularly serves the physician, provided it is approved to do premarital tests.
3. Give the laboratory the full name, complete address and age of the person from whom the blood was taken.
4. Designate that this is a premarital test.
5. If the marriage is to be out-of-state, clearly indicate the state to the laboratory. Recommend that the engaged couple see the local marriage clerk to make certain all out-of-state requirements are fulfilled.
6. If satisfied the patient is free of infectious syphilis, complete the physician's certificate when the marriage health certificate has been returned from the laboratory.
7. If the patient has syphilis, be sure the disease is not infectious before signing the certificate.

Premarital examinations provide additional opportunity (not legally required) for counseling and a general determination that the patient is in physical and mental condition for marriage.

For the nearly ten thousand Californians afflicted with severe physical handicaps, but normal mentality, life is a mixed blessing. Despite the great improvements in medical care and services, and in the social programs of our society,

many of California's severely handicapped can never hope to achieve independence. They must depend, every day, on others to perform tasks you and I take for granted.

Where will he live and who will take care of him when his own family can no longer provide a home and help with the essentials of daily living? California has no residential institutions for the mentally normal as it has for the retarded or mentally ill.

In 1965 the State Legislature authorized a four-year pilot project by the State Health Department to find solutions to these problems, to determine what residential care services are needed and how they can be provided. The Handicapped Persons Pilot Project is providing services to a representative caseload in two areas—Sacramento and Long Beach. In the first 15 months of operation, the project demonstrated that many of the residential care problems faced by the severely physically handicapped can be overcome by help from a qualified and imaginative staff, making full use of existing community programs. All needs of such persons, including assurance for continuing care, and provision for institutional care, will be determined objectively so that precise and practical recommendations can be made to the 1969 California Legislature.

An active caseload of 50 persons in each area is the project's goal. By last January, 35 severely handicapped persons in Sacramento and 19 in Long Beach were participating in the program.

CASE 1.—Mr. D was a photographer when he learned he had muscular dystrophy. In the 12 years since the original diagnosis, Mr. D has become progressively more helpless. His wife left him, partly because of the impact of his condition on the family life. His 14-year-old son and 10-year-old daughter live with him and perform all

household activities. Groceries are provided by his wife and a monthly Old Age Survivors' Disability Insurance (OASDI) benefit for the three goes mainly for rent. Mr. D either lies in bed or, if someone puts him into it, sits in a wheelchair. Unable to dress, bathe, use the bathroom or move unaided, he leaves the house only when he is taken for semi-annual trips to a clinic for reevaluation. A local physician provides limited medical care at almost no charge; twice weekly a nurse goes to his home to help bathe and care for him.

Members of the project staff obtained some housekeeping and home health aide services; a thorough medical evaluation and medical services were arranged. A new mattress and springs were purchased to replace his bed, which had broken down with continued use. With such immediate needs accommodated, the family is now formulating plans for the future—both for Mr. D and his two children.

CASE 2.—Miss A, now 40 years old, was born with cerebral palsy. As a child, she had surgical treatment and wore braces. She had periodic seizures. Until the seizures became frequent, she was taught at home. Medical advice, given more than 20 years ago, was that "nothing could be done," and the family has not sought advice since then. Miss A's aging mother is losing strength, finds it more difficult to lift, dress, feed and bathe her daughter. Savings to provide nursing home care for Miss A upon her mother's death do not seem adequate.

Members of the project staff are introducing adaptive equipment, teaching Miss A self-feeding, advising and assisting the family to use new therapies and improve physical care. Social outlets away from the mother are being arranged to give both Miss A and her mother relief from one another and more contact with others.

NEWS & NOTES

NATIONAL • STATE • COUNTY

LOS ANGELES

The American Psychiatric Association, Western Division, will hold the Western Divisional Meeting in Los Angeles 18 to 22 October 1967 at the Statler Hilton Hotel.

A scientific program of over 80 papers will cover such topics as psychotherapy in its multiple aspects; community, ethnic and cultural problems in psychiatry; somatic treatment; neurophysiological research; and psychosomatic disorders.

ORANGE

Dr. Louis A. Gottschalk will join the faculty of the University of California, Irvine-California College of Medicine 1 September as professor and chairman of the department of psychiatry and human behavior.

A medical academician for 22 years, he was formerly professor of psychiatry and coordinator of research in psychiatry at the University of Cincinnati College of Medicine.

SANTA CLARA

Three grants, two for research and one for improving a training program, were received recently by Stanford University School of Medicine.

One of the research grants was \$69,403 from the National Foundation-March of Dimes to continue searches into the causes, treatment and prevention of birth defects. Stanford operates a birth defects study center as a unit of its department of pediatrics. The center, established by the National Foundation in 1963, is directed by Dr. Norman Kretchmer, professor and executive head of the department.

The other grant for research was \$244,175 awarded by the John A. Hartford Foundation, Inc., for the study of chronic diseases and disabilities in children.

The third grant was \$21,000 awarded by the National Institute of Health to increase the number of physicians training in anesthesiology and to upgrade the quality of the training program.

GENERAL

A total of \$334,380 in new cancer research grants to California scientists—more than half of which is for study of the possible relationship of hormones to cancer—was announced recently by the California Division of the American Cancer Society.

Stanley G. Korenman, M.D., of Harbor General Hospital in Torrance received \$91,045 for a two-year investigation of the biochemical and physiological roles of estrogens and progesterones in stimulating growth and development of secondary sex tissues in the female uterus and breast.

At the University of California in San Francisco, an additional \$70,534 was awarded to C. H. Li, Ph.D., for a 12-month continuation of his already productive research into the basic structural differences of growth hormones in man and other mammals.

At the UCLA School of Medicine in Los Angeles, Stephen Zamenhof, Ph.D., was granted \$18,751 to determine whether or not the presence of growth hormone is always necessary for normal synthesis of DNA (deoxyribonucleic acid), a nucleic acid.

Three of the grants are for metabolic studies of tumors and cancer cells. They total \$69,399. Of this amount, \$32,099 goes to Dick H. Koobs, M.D., of the Loma Linda University School of Medicine for research into the metabolic differences between normal and cancer cells, and \$29,975 to Samuel Abraham, Ph.D., at Childrens Hospital Medical Center of Northern California, in Oakland, for study of the metabolism of tumors. At the University of Southern California in Los Angeles, Walter Marx, Ph.D., will receive \$7,325 for investigation of the biosynthesis of heparin, a blood anti-coagulant.

Frederic C. Ludwig, M.D., Ph.D., of the University of California San Francisco Medical Center will use a \$36,946 grant to study the relationship between radiation injury to bone marrow and leukemia virus infection.

The UCLA School of Medicine in Los Angeles was awarded a \$25,000 institutional grant for use in developing research projects at the discretion of an inter-disciplinary committee headed by Justin J. Stein, M.D.

C. J. Karzmark, Ph.D., of the Stanford University School of Medicine was awarded a \$22,705 scholar grant for research in radiologic physics and radiotherapy at the M.D. Anderson Hospital and Tumor Institute in Houston, Texas.

The Physician's BOOKSHELF



THE SKIN—A Clinicopathological Treatise—Second Edition—Arthur C. Allen, M.D., Director of Laboratories, the Jewish Hospital of Brooklyn, New York, Downstate Medical Center, Grune & Stratton, Inc., 381 Park Avenue South, New York, New York (10016), 1967. 1182 pages, 2362 illustrations, 503 full-page plates, \$48.50.

When originally published in 1954, *The Skin* by Arthur Allen was very welcome to fill the void of a text-book correlating the clinical and histologic aspects of skin disease for the confused dermatologist and pathologist alike. Since that time, Lever's text (*Dermatopathology* 1967) has given us the ultimate encyclopedia review of skin pathology, a masterful complete reference for both the dermatologist and pathologist.

These historical references are necessary in reviewing the second edition of *The Skin*. It was with disappointment that the new edition was found to have little new or different material from the original treatise. In fact, the original edition's illustrations, including monumental clinical and histologic material from the Armed Forces Institute of Pathology and other Atlas collections as well as many original photomicrographs taken by Dr. Sophie Spitz, have been darkened in their reproduction causing difficulty in seeing cell structure or a realistic clinical picture.

Many examples of deficiencies are noted. The section on anatomy of the skin presents excellent new electron microscopic photographs but is lacking in histochemistry and staining techniques of more practical importance to the clinical pathologist or dermatopathologist. The description of metabolic alterations of collagen and elastic tissue (including lipid proteinosis, myxedema and amyloid) are remarkably lacking. The distinctions between Erythema Nodosum and Erythema Induratum are only briefly commented upon. In a chapter with 24 pages of writing are lumped all verrucae, epithelial cysts, neurocutaneous syndromes and adnexal tumors. The adnexal tumors are incompletely differentiated and synonyms are not given to allow correlation with the current literature. Progress of squamous cell carcinoma is discussed with no references after 1953 and, to add to the confusion, is sub-headed under the title "laser effect on the skin."

In recent years, spindle and/or epithelioid cells have been noted to be the predominant cells of lesions categorized under the confusing title of Juvenile Melanoma and a new classification of these lesions as spindle and/or epithelioid cell nevi has been suggested. The use of specific mucopolysaccharide stains have proven to be of value in distinguishing melanoma cells from cells of Extramammary Pagets Disease. In the discussion of nevi and melanocarcinoma, Dr. Allen presents his defense against these newer viewpoints on Juvenile Melanoma and the use of staining techniques without mentioning the specific articles that would allow cross reference on this vital differentiation.

References after 1954 are scarce and new clinical and histologic photomicrographs are unfortunately few and scattered. In view of the cost (\$48.50) in relationship to the extremely poor reproduction of photographs (as contrasted to the inexpensive Armed Forces Institute of Pathology fascicles and absence of use of color (as opposed to Montgomery's text with brilliant cell detail especially on the subject of lymphomas), it is likely that this new edition will not be a welcome addition to the libraries of most dermatologists or pathologists except those engaged in research. This new edition will probably stimulate many to obtain original editions for more faithful reproductions of the original photomicrographs.

LEO INDIANER, M.D.

* * *

ROENTGEN DIAGNOSIS—VOLUME V—ABDOMEN—2nd American Edition—By H. R. Schinz, Zurich; W. E. Baensch, Washington; W. Frommhold, Berlin; R. Glauener, M.D., Stuttgart; E. Uehlinger, and J. Wellauer, Zurich, Editors—**Second American Edition**—Arranged and Edited by Leo G. Rigler, Professor of Radiology, UCLA School of Medicine, Los Angeles, Grune & Stratton, Inc., 381 Park Avenue South, New York, N.Y. 10016, 1967, 844 pages, \$55.00.

This is the first volume of the second edition to appear and is a further improvement on the outstanding reference book in diagnostic roentgenology which the previous edition was.

This volume deals with the gastrointestinal tract, including the biliary system, the liver, the spleen, inferior vena cava, the pancreas, the urinary system and the retroperitoneal lymphatic system. Short chapters on roentgen diagnosis in gynecology and obstetrics end the volume.

The illustrations are of superb quality, the material very well dealt with, the organization flawless.

The translation is excellent. The editor of the American edition, Dr. Leo Rigler, has added a few footnotes on controversial topics where there is a difference of opinion with the authors and added information not brought out in the text by them. This is a further improvement.

The authors of this volume are radiologists from Sweden, Germany, Austria and Switzerland. Many of them are new to this set of volumes; therefore, the material is not a mere bringing up-to-date from the previous edition but basically a new effort. New techniques and their applications, which have occurred since the printing of the previous edition, such as selective arteriography, lymphangiography, splenoportography, etc., are adequately discussed and beautifully illustrated.

The references are exhaustive and international and include American and English sources along with European.

This reviewer looks forward with interest and expectation to the appearance of the other four volumes.

ALEXANDER R. MARGULIS, M.D.

CURRENT PSYCHIATRIC THERAPIES—Vol. 7, 1967—
 Edited by Jules H. Masserman, M.D., Professor and Co-
 chairman of Psychiatry, Northwestern University, Chi-
 cago, Illinois. Grune & Stratton, Inc., 381 Park Avenue
 South, New York, N.Y. 10016, 1967. 251 pages, \$12.00.
 (Published annually and available in print: Vols. 1 to 6,
 dated consecutively 1961 to 1966.)

This is the seventh and latest contribution to a, by now, popular series which has appeared annually under the editorship of Dr. Jules Masserman. Its goal is to review the status of current psychiatric therapies: The title, appropriately, is cast in the plural and the reader cannot fail to be impressed by the variety and diversity of approaches now in use or of the problems to which psychiatry addresses itself and calls its own. The book follows an already familiar format and is divided into seven sections, Child and Adolescent Psychiatry, Individual Psychotherapy, Marital Therapy, Drugs and Addiction, Group Techniques, Institution and Community, and a final one, Review and Integration, with a scholarly and thoughtful article by Dr. Masserman which endeavors a synthesis of so much diversity. The topics covered in the various sections range from special and discrete issues (e.g. "Dynamically Oriented Art Therapy") to matters of broad and social import (e.g. "Developments in Community Psychiatry"). Despite its wide scope, the book does not (and could not) attempt to cover *all* facets of psychiatric thinking and interest. For example, psychoanalysis and psychosomatic medicine, which were represented in earlier issues of this series, do not appear in this volume (with the exception of one article on "Therapy of Writer's Cramp"). In general, the emphasis is on brief treatment and on group, milieu and rehabilitative approaches, in keeping with the current trend that favors interest in community psychiatry. On the whole, the quality of the individual contributions is high. Some are excellent, for example, Harold Lief's article on "Psychotherapy of Medical Students," which is thorough and quite definitive, and Elvin Semrad's on "Comprehensive Therapy of Schizophrenia." The latter in four short pages, which sparkle with Semrad's characteristically terse and lucid views, manages to describe the essentials of good treatment for the schizophrenic. One article ("Multiple Psychotherapy in Inpatient Consultation" by William Offenkrantz), on the other hand, represents what this reviewer considers innovation for its own sake. It describes the group treatment of a single patient by 8 to 18 staff members (simultaneously!).

In sum, this worthwhile addition to an already established and successful series will give the medical reader, psychiatrist and non-psychiatrist, an informative view of psychiatric thinking today.

PIETRO CASTELNUOVO-TEDESCO, M.D.

* * *

RECENT ADVANCES IN NUCLEAR MEDICINE—
 Based on a Symposium Sponsored by the Department of
 Radiology of the Hahnemann Medical College—Edited by
 Millard N. Croll, M.D., Associate Professor of Radiology;
 and Luther W. Brady, M.D., Professor of Radiology, both
 of The Hahnemann Medical College, Philadelphia. Apple-
 ton-Century-Crofts, 440 Park Ave., New York 10016, 1966.
 260 pages, \$12.50.

This book consists of a collection of papers presented at a symposium held at the Hahnemann Medical College in March 1965, covering many aspects of Nuclear Medicine. In a field progressing as actively as Nuclear Medicine, such a book can become rapidly outdated. A number of the papers included suffer from this problem, but there are several which anticipate important new developments, and several which give a good analysis of techniques currently used widely as routine procedures.

Regarding future applications, excellent papers by

Richards and by Smith outline the production, chemistry and dosimetry of technetium^{99m} which is probably becoming the most useful single isotope available to radioisotope laboratories. Harris's paper on low energy collimators also is pertinent in its applicability to technetium scanning. A paper by Charkes and his collaborators on tumor scanning with cesium¹³¹ is of interest not only for the potential usefulness of radiocesium as a tumor label, but also as an example of another generator system for isotope production. Such generators will undoubtedly be used more and more in the future.

Several papers give good detailed analysis of widely used routine tests or techniques, such as Taplin's thorough discussion of the I¹³¹-iodohippurate renocystogram, Quinn's and Taplin's comparisons of vascular and inhalatory lung scans, Johnson's analysis of kinetic data from surface counting, and Harris's comparison of methods of rate recording. Some newer and more esoteric types of tests also are well reviewed such as myocardial and cerebral blood flow studies, parathyroid scanning with Se⁷⁵-selenomethionine and its dosimetry, joint scanning, and the dosimetry of "beta-type" radiation from non-beta-emitting radionuclides.

A rather glaring omission at the symposium was the almost total absence of any reference to the Anger-type scintillation camera, an instrument which is being used more and more widely as a major scintiscanning tool. The brief paper on the auto-fluoroscope also does not go into enough detail to satisfy either the newcomer who is not familiar with its design and abilities, nor the established investigator who would like to hear more of the details of its current performance. The use of computers in Nuclear Medicine, an area which is receiving great attention and will prove extremely valuable for the storage, analysis and variable presentation of dynamic data, receives only brief comment in an article on the analysis of blood volume data. A few minor omissions suggest rather hasty editing of the book, such as reference in the first discussion to a paper which apparently was presented but not included in the published works.

In all, there are a number of useful and important articles included in the book. However, quite a few articles are too short or too superficial to be of great value. As a review the book is not fully comprehensive, omitting some important aspects of Nuclear Medicine which are of increasing current interest.

D. C. PRICE, M.D.

* * *

SYNOPSIS OF PEDIATRICS—Second Edition—By
 James G. Hughes, B.A., M.D., Professor of Pediatrics and
 Chairman of the Department of Pediatrics, University of
 Tennessee College of Medicine, Memphis, Tenn.; Chief of
 the Pediatric Service, Frank T. Tobey Memorial Child-
 ren's Hospital (City of Memphis Hospitals); Staff Mem-
 ber and former Chief of Staff of the Le Bonheur Child-
 ren's Hospital, Memphis, Tenn. With the collaboration
 of 26 faculty members of the University of Tennessee
 College of Medicine. The C. V. Mosby Company, 3207
 Washington Boulevard, St. Louis, Mo. 63103, 1967. 1,099
 pages, \$10.85.

This Synopsis of Pediatrics contains 1,099 pages. While the outside dimensions of the book are small, it is too thick and heavy for pocket or medical bag use. Its proper place is more apt to be near the desk of a general practitioner or pediatrician who wants a concise and up-to-date discussion of the diagnosis and treatment of the majority of children's diseases which are encountered in practice. It meets this need very well—but is in competition with larger and more comprehensive pediatric texts.

Many physicians, house officers and medical students will find this text quite adequate for their needs and will appreciate its more modest price.

WILLIAM C. DEAMER, M.D.

Serology of Rubella

Comparison of Fluorescent Antibody, Complement Fixation and Neutralization Tests for Diagnosis of Current Infections and Determination of Sero-immunity

EDWIN H. LENNETTE, M.D., NATHALIE J. SCHMIDT, AND
ROBERT L. MAGOFFIN, M.D., *Berkeley*

■ *Neutralization, complement fixation (CF) and indirect fluorescent antibody (FA) assays for rubella virus were compared for sensitivity in the serologic diagnosis of infection, for demonstrating antibody in the sera of infants with suspected rubella syndrome, and in the detection of antibody elicited by past infection (determination of immunity status). The combination of CF and FA tests was shown to be the most useful for serologic diagnosis of infection, largely eliminating the need for the slower and more cumbersome interference neutralization test.*

Neutralizing antibodies were found to appear rapidly in the course of infection, antibodies demonstrable by immunofluorescent staining appeared slightly later, and CF antibodies were rarely demonstrable in sera collected earlier than 14 days after onset of illness. Antibodies detected by all three techniques showed good correlation in infants with clinical evidence of rubella syndrome and corresponding maternal sera. The indirect FA technique compared favorably with the neutralization test for the detection of antibody elicited by past infection (determination of immunity status) and offered distinct advantages in ease of technical performance and more rapid results. In both current and past infections, FA titers tended to be higher than neutralizing antibody titers.

THE MEASUREMENT OF antibody levels to rubella virus has three distinct applications of clinical importance: The serologic confirmation of clinically suspected cases of rubella, the retrospective diagnosis of *in utero* infections of infants, and the determination of immunity status (sero-immunity) of pregnant women exposed to rubella infections. Neutralizing, complement-fixing and indirect fluorescent antibody assays for rubella virus have been performed in this laboratory on serum specimens obtained in such cases since April 1965. This report compares the relative value of the three test procedures for the diagnosis of current infections, describes the antibody levels in infants with clinical evidence of the rubella syndrome, and compares the sensitivity of the three techniques for detection of antibody persisting from past infection—that is, for determination of immunity status.

Materials and Methods

Neutralizing antibody assays. Tests were conducted by the interference technique in tube cultures of the BS-C-1 line of grivet monkey kidney cells. Two-fold dilutions of inactivated (56°C for 30 minutes) serum, ranging from 1:4 through 1:64 were tested against approximately ten 50 per cent interfering doses (InD₅₀) of rubella virus. The inoculated cultures were challenged with 100 TCD₅₀ of echovirus type 11 after five days' incubation at 36°C, and results were read two to four days later. Neutralization of the rubella virus was evidenced by a cytopathic effect (CPE) produced by the echovirus, while failure of the test serum to neutralize the rubella virus was indicated by a lack of echovirus CPE (interference).

Complement-fixing (CF) antibody assays. Sera were examined for the presence of rubella CF antibodies by the standard technique of this laboratory adapted to use with the microtiter system.⁴ Antigens were prepared from the fluid phase of infected RK-13 (rabbit kidney) cell cultures⁷ or BHK-21 (hamster kidney) cell cultures.⁸ Infected fluids were concentrated 100-fold by dialysis against polyethylene glycol and the concentrates were treated with one-half volume of anesthetic ether for one hour at room temperature. After

centrifugation at 1,500 rpm for 15 minutes the aqueous phase was removed for use as CF antigen. Residual ether was removed by bubbling with nitrogen. Sera (inactivated at 60°C for 30 minutes) were tested at two-fold dilutions ranging from 1:4 through 1:32 against two units of antigen (as determined by block titrations).

Indirect fluorescent antibody (FA) assays. The indirect immunofluorescent staining technique of this laboratory for detection of rubella antibodies is described in detail elsewhere.⁵ Briefly, smears of infected BS-C-1 cells (and uninfected cells for control purposes) were fixed with acetone and ringed with quick-drying paint.* Test sera were inactivated at 56° for 30 minutes, and two-fold dilutions ranging from 1:4 through 1:128 were prepared in a 20 per cent suspension of normal beef brain (to reduce nonspecific staining and overstaining). A drop of each serum dilution was applied to a smear of infected cells, and the lower dilutions were also tested against smears of uninfected cells. After incubation at 36°C for 20 minutes in a humidified atmosphere, slides were washed multiple times in phosphate buffered saline solution (PBS), pH 7.2 to 7.4. The combination of specific antibodies in the test serum with rubella virus antigen in the infected cells was detected through the use of fluorescein-labeled anti-human immune globulins prepared in rabbits. The conjugate, diluted appropriately in a 20 per cent suspension of beef brain, was added to the smears and the slides were then incubated at 36°C for 20 minutes. After washing, the smears were mounted in a 25 per cent solution of glycerol in PBS, pH 7.3. The equipment employed in the examination of smears for immunofluorescent staining has been described previously.⁵ Antibody titers were expressed in terms of the highest dilution of test serum which gave specific immunofluorescent staining with the rubella-infected cells.

*Manufactured by Tri-Chem, Inc., Belleville, N. J.

TABLE 1.—Results of Neutralizing, (Neut.), Complement-Fixing (CF) and Fluorescent Antibody (FA) Determinations in Cases of Suspected Rubella.

| Type of test | Total cases* | Rise in titer, 4-fold or greater | No rise in titer, antibody present | No antibody (<1:4) |
|--------------|--------------|----------------------------------|------------------------------------|--------------------|
| CF | 114 | 45 | 36 | 33 |
| Neut. | 114 | 37 | 55 | 22 |
| FA | 114 | 51 | 37 | 26 |

*Cases with satisfactory paired sera tested; acute-phase serum taken within seven days, convalescent-phase serum taken 14 or more days after onset.

From the Viral and Rickettsial Disease Laboratory, California State Department of Public Health.

The work on which this report is based was supported by Grant AI-01475 from the National Institute of Allergy and Infectious Diseases, National Institutes of Health, United States Public Health Service, Department of Health, Education and Welfare.

Submitted 24 February 1967.

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Results

Comparative diagnostic value of neutralization, complement fixation and indirect fluorescent antibody tests. Antibody responses demonstrated by neutralization, CF and FA tests in 114 suspected clinical cases of rubella in which suitable paired serum specimens were obtained are summarized in Table 1. "Paired" specimens were considered satisfactory for diagnosis if the acute-phase serum was collected no later than seven days after onset of illness and the convalescent-phase serum was taken 14 or more days after onset. This group of cases was made up predominantly of pregnant women or their contacts, mostly children, but included a few college students.

The FA test detected significant antibody increases (four-fold or greater rise in titer) in the greatest number of patients, the CF test in slightly fewer, and the neutralization test in the fewest. When the results of the three tests were collated (Table 2), a total of 61 patients showed a diagnostic rise in antibody titer by one or more tests. Of these, only 25 showed positive results in all three tests. In 22 cases, two of the tests were positive, most often by the CF and FA tests, and in 14 instances only a single test was positive. In the latter group, the FA test was positive in seven cases, the CF test in five and the neutralization test in two. Considering the results of any pair of tests independently, slightly more cases were con-

TABLE 2.—Comparative Frequency of Positive Results by Complement Fixation, Neutralization and Fluorescent Antibody Tests in 114 Suspected Cases of Rubella.

| Combinations of tests showing antibody | Number of cases with | |
|----------------------------------------|-------------------------------------------|------------------------------------|
| | Rise in antibody titer, 4-fold or greater | No rise in titer, antibody present |
| One or more tests | 61 | 34 |
| All three tests | 25 | 23 |
| Two tests only | | |
| CF and neut. | 3 | 2 |
| CF and FA | 12 | 0 |
| FA and neut. | 7 | 3 |
| One test only | | |
| CF | 5 | 0 |
| Neut. | 2 | 4 |
| FA | 7 | 2 |
| Each test independently | | |
| CF | 45 | 25 |
| Neut. | 37 | 32 |
| FA | 51 | 31 |
| Two tests independently | | |
| CF and/or neut. | 55 | 32 |
| CF and/or FA | 59 | 30 |
| FA and/or neut. | 56 | 34 |

Code: Neut.=Neutralizing; CF=Complement Fixing; FA=Fluorescent Antibody.

TABLE 3.—Correlation of Results of Complement Fixation, Neutralization and Fluorescent Antibody Tests in Cases of Suspected Clinical Rubella.

| CF Against Neutralization Test | | | | |
|---------------------------------|-----------------|-----------------------------|-------------------------|-----------------|
| CF test results | Number of cases | Neutralization test results | | |
| | | Rise in titer, 4-fold or > | No rise, titer 1:4 or > | Negative (<1:4) |
| Rise in titer, 4-fold or >..... | 45 | 28 | 17 | 0 |
| No rise, titer 1:4 or > | 36 | 6 | 30 | 0 |
| Negative <1:4 | 33 | 3 | 8 | 22 |
| Totals | 114 | 37 | 55 | 22 |

| CF Against FA Test | | | | |
|---------------------------------|-----------------|----------------------------|-------------------------|-----------------|
| CF test results | Number of cases | FA test results | | |
| | | Rise in titer, 4-fold or > | No rise, titer 1:4 or > | Negative (<1:4) |
| Rise in titer, 4-fold or >..... | 45 | 37 | 8 | 0 |
| No rise, titer 1:4 or > | 36 | 9 | 24 | 3 |
| Negative <1:4 | 33 | 5 | 5 | 23 |
| Totals | 114 | 51 | 37 | 26 |

| FA Against Neutralization Test | | | | |
|---------------------------------|-----------------|-----------------------------|-------------------------|-----------------|
| FA test results | Number of cases | Neutralization test results | | |
| | | Rise in titer, 4-fold or > | No rise, titer 1:4 or > | Negative (<1:4) |
| Rise in titer, 4-fold or >..... | 51 | 32 | 18 | 1 |
| No rise, titer 1:4 or > | 37 | 4 | 31 | 2 |
| Negative <1:4 | 26 | 1 | 6 | 19 |
| Totals | 114 | 37 | 55 | 22 |

Code: Neut.=Neutralizing; CF=Complement Fixing; FA=Fluorescent Antibody.

firmed by the CF and/or FA tests than by other pairs of tests.

Correlation between neutralizing, complement-fixing and indirect FA responses in clinical rubella. The correlation of positive, inconclusive, and negative findings with the three test procedures in the 114 suspected cases of rubella is shown in Table 3.

The CF and the FA tests each detected significant antibody increases in a number of patients (17 and 18 cases respectively) who showed stationary titers of neutralizing antibody. The converse—neutralizing antibody titer rises missed by CF or FA—occurred much less often (nine and five cases respectively). None of the patients showed CF antibody in the absence of neutralizing

TABLE 4.—*Complement Fixation, Neutralization and Fluorescent Antibody Titers of Patients Showing Significant Antibody Titer Rises in Only a Single Test.*

| Patient | Days after onset | Antibody titer | | | Patient | Days after onset | Antibody titer | | |
|---------|------------------|----------------|-------|-----|---------|------------------|----------------|-------|-----|
| | | CF | Neut. | FA | | | CF | Neut. | FA |
| 1..... | 6 | <4 | 8 | 64 | 8..... | 2 | <4 | 8 | <4 |
| | 34 | 16 | 8 | 128 | | 19 | <4 | 8 | 64 |
| 2..... | 5 | <4 | 64 | 128 | 9..... | 2 | <4 | 8 | <4 |
| | 21 | 16 | 32 | 128 | | 16 | 4 | 8 | 128 |
| 3..... | 7 | <4 | 16 | 64 | 10..... | 3 | <4 | 4 | <4 |
| | 26 | 16 | 32 | 128 | | 17 | 4 | 8 | 128 |
| 4..... | 5 | <4 | 64 | 64 | 11..... | 2 | <4 | 4 | 4 |
| | 21 | 32 | 32 | 64 | | 22 | <4 | <4 | 16 |
| 5..... | 1 | <4 | 16 | 64 | 12..... | 6 | <4 | 16 | <4 |
| | 14 | 8 | 16 | 64 | | 15 | 4 | 16 | 16 |
| 6..... | 3 | 8 | 8 | 64 | 13..... | 1 | <4 | 16 | <4 |
| | 23 | 16 | 64 | 64 | | 15 | 4 | 16 | 16 |
| 7..... | 2 | <4 | <4 | <4 | 14..... | 2 | <4 | <4 | <4 |
| | 37 | 4 | 32 | <4 | | 17 | 4 | 4 | 64 |

Code: Neut.=Neutralizing; CF=Complement Fixing; FA=Fluorescent Antibody.

antibody; FA antibody was present in three cases without neutralizing antibody.

The CF test detected antibody titer increases missed by the FA tests in eight patients; the FA test was positive in 14 patients showing no rise in CF antibody titer, including five with no demonstrable CF antibody.

To illustrate some of the divergent results obtained with the three tests, Table 4 shows the antibody levels of the 14 patients who had significant titer rises demonstrated by a single test. In four of the five patients (Nos. 1 to 5) with titer rises shown only by the CF test, the acute-phase sera were collected five to seven days after onset. Neutralization and FA titers were already relatively high and remained stationary or changed only two-fold, while CF antibody, which appears more slowly (see Table 6), showed significant increases in titer.

Both of the two patients (Nos. 6 and 7) with

diagnostically significant rises in antibody level shown only in neutralization tests, had two-fold increases in CF antibody; one showed a stationary FA titer, while the other had no demonstrable fluorescent antibody.

Of the seven patients (Nos. 8 to 14) showing significant titer rises only in FA tests, five had low neutralizing antibody titers which remained stationary or changed only two-fold. Borderline CF titer increases of from less than 1:4 to 1:4 were also demonstrated in five of the patients.

The range of neutralizing, CF and fluorescent antibody titers elicited by rubella infections is shown in Table 5 which correlates the FA titers of convalescent-phase serum specimens with neutralizing and CF antibody titers. These convalescent-phase sera are from the 61 persons shown in Table 2 with serologic evidence of rubella infection by one or more tests. The most frequently-occurring CF titers were 1:8 and 1:16, while

TABLE 5.—*Correlation of Fluorescent Antibody Titers with Neutralization and Complement Fixation Antibody Titers in Convalescent-Phase Serum Specimens.**

| CF antibody titer | No. of sera | FA titer | | | | | | |
|-------------------|-------------|----------|------|------|------|------|----|------|
| | | <4 | 4 | 8 | 16 | 32 | 64 | ≥128 |
| ≥32..... | 7 | | | | | | 3 | 4 |
| 16..... | 19 | | | | 1 | 3 | 7 | 8 |
| 8..... | 22 | | | | 1 | 2 | 9 | 10 |
| 4..... | 8 | 1 | | | 2 | | 1 | 4 |
| <4..... | 5 | | | | 2 | 1 | 2 | |
| Totals | 61 | 1 | 0 | 0 | 6 | 6 | 22 | 26 |

| Neut. antibody titer | No. of sera | FA titer | | | | | | |
|----------------------|-------------|----------|------|------|------|------|------|------|
| | | <4 | 4 | 8 | 16 | 32 | 64 | ≥128 |
| ≥64..... | 8 | | | | | | 3 | 5 |
| 32..... | 14 | 1 | | | | 2 | 6 | 5 |
| 16..... | 26 | | | | 3 | 3 | 8 | 12 |
| 8..... | 8 | | | | 2 | 1 | 3 | 2 |
| 4..... | 4 | | | | | | 2 | 2 |
| <4..... | 1 | | | | 1 | | | |
| Totals | 61 | 1 | 0 | 0 | 6 | 6 | 22 | 26 |

*Sera from 61 patients showing serologic evidence of rubella infection by one or more test.
Code: Neut.=Neutralizing; CF=Complement Fixing; FA=Fluorescent Antibody.

TABLE 6.—Antibody Titers Relative to Time After Onset of Illness in 64 Serologically Confirmed Cases of Rubella.

| | Number of sera with antibody shown by CF test Days after onset—64 cases | | | | | | Number of sera with antibody shown by Neutralization test Days after onset—64 cases | | | | | | Number of sera with antibody shown by FA test Days after onset—64 cases | | | | | |
|-------|-------------------------------------------------------------------------------|------|------|-------|-------|------|-------------------------------------------------------------------------------------------|------|------|-------|-------|------|-------------------------------------------------------------------------------|------|------|-------|-------|------|
| | 0-3 | 4-7 | 8-13 | 14-20 | 21-27 | 28> | 0-3 | 4-7 | 8-13 | 14-20 | 21-27 | 28> | 0-3 | 4-7 | 8-13 | 14-20 | 21-27 | 28> |
| | Antibody titer | | | | | | | | | | | | | | | | | |
| ≥ 128 | | | | | | | | 2 | | 4 | 3 | 1 | | 2 | 2 | 17 | 7 | 2 |
| 64 | | | | | | | | 2 | | 4 | 3 | 1 | 3 | 4 | | 14 | 8 | 1 |
| 32 | | | | 2 | 4 | 1 | | 1 | 1 | 9 | 4 | | | 1 | | 6 | | |
| 16 | | | | 13 | 4 | 2 | 6 | 7 | 2 | 19 | 7 | 1 | | 2 | 1 | 4 | 2 | |
| 8 | 1 | 1 | 1 | 16 | 6 | | 4 | 4 | 1 | 7 | 2 | 1 | 2 | | | | | |
| 4 | 1 | | 1 | 7 | 1 | | 6 | 2 | | 3 | | | 5 | 1 | | | | |
| < 4 | | | | | | | | | | | | | | | | | | |
| < 8 | 41 | 19 | 2 | 3 | 2 | | 27 | 4 | | | 1 | | 33 | 10 | 1 | | | |

Code: Neut.=Neutralizing; CF=Complement Fixing; FA=Fluorescent Antibody.

neutralization titers tended to be one dilution (two-fold) higher, most commonly 1:16 and 1:32. However, in FA tests most of the sera showed titers of 1:64 or 1:128 or greater. A single serum showed neutralizing and CF antibody, but no antibody was demonstrable in the FA test.

Temporal appearance of rubella antibody. Table 6 shows CF, neutralizing and FA titers relative to the time after onset of illness in serologically confirmed cases of rubella. Data were available on 64 patients, including three whose serum specimens were not collected at the recommended times (see footnote, Table 1), but who showed significant rises in rubella antibody titer by one or more tests. This table illustrates the relatively slow development of CF antibody. Only three of the 63 sera collected within seven days after onset showed CF antibody; whereas, neutralizing antibody was demonstrable in 32 of these "acute-phase" sera, including 16 of the 43 sera obtained within three days after onset. The frequency of antibody demonstrable by the FA test within the first week after onset was intermediate (in ten of

the 43 sera collected at 0 to 3 days and in ten of the 20 sera collected at 4 to 7 days), probably reflecting a somewhat slower development than neutralizing antibody. However, titers of fluorescent antibody were generally higher than neutralizing antibody levels. Thus, the greater diagnostic value of the CF and FA tests as compared to the neutralization test may be attributable to a slower development of CF and FA antibody, and the higher titers demonstrable by the FA test may account for the ability of this technique to demonstrate diagnostically significant increases in antibody in cases in which CF test shows inconclusive titer increases, for example, less than 1:4 to 1:4 (see Table 4).

Antibody levels in infants with suspected rubella syndrome. Sera from a total of 106 infants with suspected intra-uterine infections were examined by the three antibody assay techniques. In Table 7 it is seen that 89 of the infants showed antibody in one or more tests while 17 did not show antibody by any of the test procedures. Neutralizing and fluorescent antibodies were de-

TABLE 7.—Comparison of Complement Fixation, Neutralization and Fluorescent Antibody Tests for Demonstration of Antibody to Rubella in Infants with Suspected Intra-uterine Infection.

| Tests showing antibody present | Number of infants by age at time serum was collected | | | | | |
|-----------------------------------|------------------------------------------------------|---------|---------|---------|------------|---------|
| | Total | 0-1 mo. | 2-3 mo. | 4-6 mo. | over 6 mo. | unknown |
| Total, any test | 89 | 61 | 20 | 4 | 2 | 2 |
| All three tests | 59 | 45 | 10 | 1 | 2 | 1 |
| Two tests only | (24) | (14) | (6) | (3) | | (1) |
| CF and neut. | 1 | | 1 | | | |
| CF and FA | | | | | | |
| Neut. and FA | 23 | 14 | 5 | 3 | | 1 |
| One test only | (6) | (2) | (4) | | | |
| CF | | | | | | |
| Neut. | 2 | 1 | 1 | | | |
| FA | 4 | 1 | 3 | | | |
| Each test independently | | | | | | |
| CF | 60 | 45 | 11 | 1 | 2 | 1 |
| Neut. | 85 | 60 | 17 | 4 | 2 | 2 |
| FA | 86 | 60 | 18 | 4 | 2 | 2 |
| All tests negative | 17 | 6 | 7 | 2 | 2 | |
| Total cases | 106 | 67 | 27 | 6 | 4 | 2 |

Code: Neut.=Neutralizing; CF=Complement Fixing; FA=Fluorescent Antibody.

monstrable in more infants than was CF antibody, but of the 89 infants showing neutralizing and/or fluorescent antibody, 60 also had detectable CF antibody.

Table 8 compares antibody titers obtained in the three test systems with sera of 81 infants (0 to 3 months of age) who had antibody demonstrable by one or more tests. A number of sera with high levels of neutralizing or fluorescent antibody had no CF antibody. This may, in part, reflect the rapid decline of the CF antibody titer of the mother, and therefore of passively-acquired CF antibody of the infant, in the interval between infection and delivery and the inability of some infants to produce CF antibody during the first few weeks of life. Also, some of the sera were from infants with questionable symptoms and questionable histories of maternal rubella infections; in these the neutralization and fluorescent antibody titers could well represent residual antibody from an earlier maternal infection with subsequent loss of CF anti-

TABLE 8.—*Comparison of Rubella Antibody Titers Demonstrated by Complement Fixation, Neutralization and Fluorescent Antibody Tests on Sera of 81 Infants (0-3 Months of Age) with Suspected Intra-uterine Infections.**

| Neut. titer | No. of infants | CF antibody titer | | | | |
|--------------|----------------|-------------------|------|------|------|------|
| | | <4 | 4 | 8 | 16 | ≥32 |
| ≥64..... | 23 | 2 | 3 | 2 | 12 | 4 |
| 32..... | 23 | 6 | 5 | 5 | 4 | 3 |
| 16..... | 15 | 6 | 3 | 4 | 2 | |
| 8..... | 8 | 4 | 2 | 2 | | |
| 4..... | 8 | 3 | 5 | | | |
| <4..... | 4 | 4 | | | | |
| Totals | 81 | 25 | 18 | 13 | 18 | 7 |

| FA titer | No. of infants | CF antibody titer | | | | |
|--------------|----------------|-------------------|------|------|------|------|
| | | <4 | 4 | 8 | 16 | ≥32 |
| ≥128..... | 28 | 6 | 4 | 4 | 8 | 6 |
| 64..... | 17 | 4 | | 5 | 8 | |
| 32..... | 13 | 4 | 6 | 1 | 1 | 1 |
| 16..... | 11 | 3 | 5 | 3 | | |
| 8..... | 6 | 3 | 2 | | 1 | |
| 4..... | 3 | 3 | | | | |
| <4..... | 3 | 2 | 1 | | | |
| Totals | 81 | 25 | 18 | 13 | 18 | 7 |

| Neut. titer | No. of infants | FA titer | | | | | | |
|--------------|----------------|----------|------|------|------|------|------|------|
| | | <4 | 4 | 8 | 16 | 32 | 64 | ≥128 |
| ≥64..... | 23 | | | 1 | | 2 | 4 | 16 |
| 32..... | 23 | 1 | | | 4 | 5 | 7 | 6 |
| 16..... | 15 | | | 3 | 2 | 3 | 4 | 3 |
| 8..... | 8 | 1 | 3 | | 2 | | | 2 |
| 4..... | 8 | 1 | | | 2 | 3 | 1 | 1 |
| <4..... | 4 | | | 2 | 1 | | 1 | |
| Totals | 81 | 3 | 3 | 6 | 11 | 13 | 17 | 28 |

*Infants having antibody demonstrated by one or more tests.

TABLE 9.—*Correlation of Rubella Antibody Titers Demonstrated by Complement Fixation, Neutralization and Fluorescent Antibody Tests on Maternal and Infant Sera in 30 Cases of Suspected Intra-uterine Infection.**

| CF Test | | | | | | | |
|-------------------|-----------------|-----------------------|-----|-----|-----|-----|-----|
| Mother's titer | No. of cases | Baby's antibody titer | | | | | |
| | | <4 | 4 | 8 | 16 | 32 | 64 |
| 64..... | --- | --- | --- | --- | --- | --- | --- |
| 32..... | 3 | --- | --- | 1 | 1 | 1 | --- |
| 16..... | 4 | 1 | --- | 1 | 2 | --- | --- |
| 8..... | 7 | 1 | --- | 3 | 2 | 1 | --- |
| 4..... | 7 | 1 | 2 | 3 | 1 | --- | --- |
| <4..... | 9 | 9 | --- | --- | --- | --- | --- |
| Totals | 30 | 12 | 2 | 8 | 6 | 2 | --- |

| Neutralization Test | | | | | | | |
|---------------------|-----------------|-----------------------|-----|-----|-----|-----|-----|
| Mother's titer | No. of cases | Baby's antibody titer | | | | | |
| | | <4 | 4 | 8 | 16 | 32 | 64 |
| 64..... | 5 | --- | --- | --- | --- | 1 | 4 |
| 32..... | 5 | --- | --- | 1 | 1 | 2 | 1 |
| 16..... | 9 | --- | 1 | --- | 3 | 2 | 3 |
| 8..... | 4 | --- | 1 | 2 | --- | 1 | --- |
| 4..... | 3 | 2 | 1 | --- | --- | --- | --- |
| <4..... | 4 | 2 | --- | 1 | 1 | --- | --- |
| Totals | 30 | 4 | 3 | 4 | 5 | 6 | 8 |

| FA Test | | | | | | | | |
|-------------------|-----------------|-----------------------|-----|-----|-----|-----|-----|------|
| Mother's titer | No. of cases | Baby's antibody titer | | | | | | |
| | | <4 | 4 | 8 | 16 | 32 | 64 | ≥128 |
| ≥128..... | 6 | --- | --- | --- | 1 | --- | --- | 5 |
| 64..... | 12 | --- | 1 | --- | --- | 3 | 4 | 4 |
| 32..... | 4 | --- | --- | --- | --- | 1 | 3 | --- |
| 16..... | 1 | --- | --- | --- | 1 | --- | --- | --- |
| 8..... | 1 | --- | --- | --- | 1 | --- | --- | --- |
| 4..... | 1 | --- | --- | --- | 1 | --- | --- | --- |
| <4..... | 5 | 3 | 2 | --- | --- | --- | --- | --- |
| Totals | 30 | 3 | 3 | --- | 4 | 4 | 7 | 9 |

*Sera obtained within one month of birth from mother and infant.

Code: Neut.=Neutralizing; CF=Complement Fixing; FA=Fluorescent Antibody.

body. FA titers of the infants' sera tended to be somewhat higher than the neutralization titers.

In Table 9 neutralizing, CF and fluorescent antibody titers of infants less than one month of age are compared with antibody titers of their mothers' sera taken at, or about, the same time. Correlation of all three types of antibody is seen to be fairly good. In both the mothers' and infants' sera CF antibody was less often demonstrable than fluorescent or neutralizing antibody but in some instances the infants' CF antibody titers exceeded those of their mothers.

It has been shown that rubella neutralizing antibody persists in congenitally-infected infants long after maternally-acquired antibody normally

is lost, possibly for life.^{3,9} However, the neutralizing antibody has been found to undergo changes in physicochemical properties, consisting largely of 7S globulins at birth, presumably of maternal origin; these antibodies diminish and are replaced by 19S antibody which reaches maximum levels at four to seven months. The 19S antibody is then replaced by 7S antibody which may persist throughout life.^{1,2} It would appear that information of some diagnostic value might be gained by the examination of a serum specimen taken shortly after birth together with one taken after maternal antibody would normally have disappeared. If antibody is present in the first specimen but absent or declining in the second, it is probably of maternal origin, but if antibody persists after the time at which maternal antibody normally is lost, it is likely to have been produced by the infant in response to a chronic, congenitally-acquired infection.

Dual serum specimens were examined from 20 infants with suspected rubella syndrome; three of these infants had no antibody in either specimen and in six cases the specimens were collected too close together for a comparison of antibody titers to have meaning. Results of antibody assays and virus isolation attempts on the 11 infants with suitably-spaced serum specimens are presented in

TABLE 10.—Results of Virus Isolation Attempts and Antibody Assays on Sera of Infants with Suspected Rubella Syndrome.

| Patient | Sex | Virus isol. | Time after birth | Antibody titer | | |
|---------|-----|-------------|------------------|----------------|-------|-----|
| | | | | CF | Neut. | FA |
| 1..... | F | + | 4 days | 8 | 16 | 64 |
| | | | 1 month | 4 | 8 | 64 |
| 2..... | F | + | 2 months | <4 | 32 | 128 |
| | | | 4 months | <4 | 64 | 128 |
| 3..... | F | + | 1 day | 4 | 16 | 128 |
| | | | 1 month | 4 | 32 | 128 |
| 4..... | F | + | 2 weeks | <4 | 16 | 128 |
| | | | 1 month | 4 | 32 | 128 |
| 5..... | M | + | 7 weeks | 16 | 64 | 128 |
| | | | 3.5 months | 8 | 64 | 128 |
| 6..... | M | 0 | 2 days | 16 | 64 | 128 |
| | | | 2 months | 16 | 32 | 128 |
| 7..... | F | 0 | 3 months | <4 | 16 | 8 |
| | | | 4 months | <4 | 8 | <4 |
| 8..... | M | 0 | 4 days | 4 | 32 | 16 |
| | | | 2.5 months | 4 | 4 | <4 |
| 9..... | M | 0 | 1 month | 4 | 8 | 16 |
| | | | 4 months | <4 | 4 | <4 |
| 10..... | F | 0 | 7 weeks | 8 | 8 | 16 |
| | | | 6 months | <4 | <4 | <4 |
| 11..... | F | 0 | 2 weeks | 16 | 64 | 128 |
| | | | 6 weeks | <4 | 4 | 32 |

Code: Neut.=Neutralizing; CF=Complement Fixing; FA=Fluorescent Antibody.

TABLE 11.—Antibody from Past Rubella Infections Detected by Complement Fixation, Neutralization and Indirect Fluorescent Antibody Tests. Sera from 117 Persons Obtained at Time of Exposure.

| Antibody detected by: | Number of persons with detectable antibody |
|----------------------------|--------------------------------------------|
| Total, any test | 96 |
| All three tests | 69 |
| Two tests only | (16) |
| CF and neut. | 1 |
| CF and FA | 0 |
| Neut. and FA | 15 |
| One test only | (11) |
| CF | 1 |
| Neut. | 7 |
| FA | 3 |
| Each test independently | |
| CF | 71 |
| Neut. | 92 |
| FA | 87 |
| All tests negative..... | 21 |
| Total persons tested | 117 |

Code: Neut.=Neutralizing; CF=Complement Fixing; FA=Fluorescent Antibody.

Table 10. Five of the infants (Nos. 1 to 5) yielded virus in their throat washings, and it is seen that their antibody levels remained stationary (or changed no more than two-fold) for one to four months after birth. Patient No. 6 had a negative virus isolation attempt, but the persistence of all three kinds of antibody suggests a congenital infection. Neutralizing and fluorescent antibody levels of the first six patients were generally higher than those for patients Nos. 7 to 11, whose antibody appears to have been solely of maternal origin since it had disappeared or decreased sharply by the time the second specimen was taken. The results of tests on this small number of infants indicate that antibody assays on suitably spaced serum specimens may aid in the retrospective diagnosis of infection with rubella virus *in utero*.

Comparative sensitivity of neutralization, FA and CF tests for demonstration of antibody elicited by past infections. To compare the sensitivity of the three tests for detection of antibody elicited by past infection, sera were examined from individuals who had been exposed to rubella but had no clinical evidence of infection. Antibodies in these sera, collected within a few days of exposure, were considered to have been produced in response to past infection. In Table 11, it is seen that of 117 post-exposure sera examined, 96 showed antibody by one or more test procedures, while 21 did not show antibody in any test. The neutralization test, which detected antibody in 92 sera, was the most sensitive; the FA test was only

slightly less sensitive, detecting antibody in 87 sera. The CF test detected antibody in approximately 74 per cent of the sera showing neutralizing and/or fluorescent antibody. The single individual who had rubella antibody demonstrable only in the CF test had a titer of 1:4; this is the only serum specimen out of hundreds tested which showed CF antibody in the absence of neutralizing or fluorescent antibody.

The sensitivity of the neutralization and FA tests for detecting antibody from past infections is further compared in Table 12, which shows the antibody titers demonstrated by each test in two groups of persons. The first group consisted of 93 persons with antibody demonstrable in sera collected at the time of exposure, and the second of 33 who had illnesses clinically suspicious of rubella but who had antibody in their acute-phase serum specimens and did not show increases in antibody titer. These persons are considered to have had past, but not current, infections with rubella virus. In both groups of sera, the FA titers tended to be higher than neutralizing antibody titers, but in each group there were a few more persons with antibody detected by the neutralization test only, than by the FA test only.

Discussion

The clinical diagnosis of rubella is often equivocal; hence, a reliable serologic test to confirm sus-

pected infections in pregnant women offers the physician a more secure basis for decisions regarding the management of the pregnancy. Fairly often, however, the time required to obtain the laboratory result seriously limits its usefulness to the physician. The neutralization test, while providing a generally accepted standard against which other serologic tests may be compared for sensitivity and specificity, requires at least a week, often ten to fourteen days, to perform after the test sera are in hand and previously prepared cell cultures are ready for inoculation. The CF and FA tests can be completed in one or two days and, equally important, are more adaptable for setting up new test-runs several times weekly. Thus, if equally reliable, the CF and FA methods both possess distinct advantages in time and ease of performance over the more cumbersome neutralization procedure.

In these studies the CF and indirect FA tests were about equally useful for the serologic diagnosis of current rubella virus infections. The use of both tests provided the most effective diagnostic approach and this is the current practice in this laboratory. The FA test, in our hands, is more sensitive than the CF test in detecting specific antibody, and in certain instances it may demonstrate a significant rise in antibody titer while the CF test remains negative or shows an equivocal increase in titer from less than 1:4 to 1:4. On the

TABLE 12.—*Correlation of Fluorescent Antibody and Neutralization Antibody Titers of Individuals with Past Rubella Virus Infections.*

| A. 93 Individuals with Antibody at Time of Exposure | | | | | | | | |
|-----------------------------------------------------------------------------------------------------|----------------|----------|------|------|------|------|------|------|
| Neut. titer | No. of sera | FA titer | | | | | | |
| | | <4 | 4 | 8 | 16 | 32 | 64 | ≥128 |
| ≥64..... | 11 | 1 | | | 1 | 4 | 3 | 2 |
| 32..... | 20 | | | | 2 | 5 | 9 | 4 |
| 16..... | 25 | 1 | 1 | 2 | 6 | 7 | 4 | 4 |
| 8..... | 21 | 3 | | 2 | 6 | 6 | 4 | |
| 4..... | 13 | 2 | 1 | 6 | 1 | 3 | | |
| <4..... | 3 | | 1 | | | 2 | | |
| Totals | 93 | 7 | 3 | 10 | 16 | 27 | 20 | 10 |
| B. 33 Patients with Suspected Clinical Rubella who Showed Antibody in Acute-phase Illness Specimens | | | | | | | | |
| Neut. titer | No. of sera | FA titer | | | | | | |
| | | <4 | 4 | 8 | 16 | 32 | 64 | ≥128 |
| ≥64..... | 3 | | | | 1 | | 1 | 1 |
| 32..... | 6 | 1 | | | 1 | 3 | 1 | |
| 16..... | 12 | 1 | | 2 | | 5 | 1 | 3 |
| 8..... | 7 | 2 | | 1 | | 3 | 1 | |
| 4..... | 3 | 1 | | 1 | 1 | | | |
| <4..... | 2 | | | 1 | | | 1 | |
| Totals | 33 | 5 | 0 | 5 | 3 | 11 | 5 | 4 |

Code: Neut.=Neutralizing; CF=Complement Fixing; FA=Fluorescent Antibody.

other hand, CF antibody is slower to appear than antibody detectable by immunofluorescent staining; hence, in some cases in which the acute-phase serum specimen is not collected promptly, fluorescent antibody may have already reached high levels and not increase further, while CF antibody shows a significant titer rise. As neutralizing antibody usually appears earlier and reaches maximal titers sooner than either FA or CF antibody, neutralization tests have rarely demonstrated significant titer rises missed by the other two tests.

Sever and coworkers⁶ have reported a less favorable experience with FA tests. On three of the four examples of antibody responses in rubella given in their report, neutralizing and CF antibody titers showed significant increases during the course of the illness, but FA titers were at high levels on the first or second day of the rash, and significant increases in FA titer could not be demonstrated. The first specimens on their patients were taken *before* infection, and thus seroconversion was demonstrated by all tests. In our studies, however, fluorescent antibody appeared slightly later than neutralizing antibody, so that significant increases were demonstrable by the FA test in a number of patients whose neutralizing antibody titers were already elevated in the acute-phase specimens (this was seen in 18 of 51 cases confirmed by FA tests).

Studies on the small number of infants in our series with suitably-spaced serum specimens indicate that antibody assays on a serum specimen taken soon after birth together with one taken several months later, when maternal antibody would normally have disappeared, may aid in the diagnosis of congenitally-acquired infections. In infants with chronic infections acquired *in utero*, antibody levels persist. The FA or neutralization test would appear to be most useful for this purpose, since in some instances CF antibody was absent or at low levels. Sever and coworkers⁶ noted that the CF titers of infants infected *in utero* decline between one to five months following birth, but that after the fifth month CF antibody levels increase, frequently exceeding those seen at the time of birth. None of the infants' sera examined in our studies were collected at appropriate times to demonstrate such a decline and reappearance of CF antibody.

From these investigations it would appear that the FA test is adequately sensitive for detection of antibody elicited by past infection—that is, for determination of immunity status. Sera taken at

the time of exposure showed neutralizing antibody without corresponding fluorescent antibody slightly more often than *vice versa*, but on the other hand FA titers tended to be higher than neutralizing antibody titers. While more extensive information on the persistence of fluorescent antibody as compared with that of neutralizing antibody is needed, from the data thus far obtained we believe the technical advantages of the FA method outweigh its slightly lesser sensitivity. FA tests are less cumbersome and expensive to perform than are interference neutralizing tests, they are beset with fewer variables, endpoints are more reproducible and results can be obtained more rapidly. While CF antibody was not demonstrable in about 25 per cent of post-exposure sera showing antibody in neutralization and/or FA tests, the CF test can be useful for rapid screening for the determination of immunity status, leaving the minority of sera failing to show CF antibody to be further examined in FA or neutralization tests. The CF test proved to be highly specific; only a single serum specimen out of hundreds examined had CF antibody (a low titer of 1:4) in the absence of neutralizing or fluorescent antibody.

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A Hard Look at the Future of Family Practice

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■ *The progressive fall in the status and numbers of general practitioners has produced a dangerous void in the field of comprehensive medical care. The Millis Commission and other national study committees have recommended that family practice be made a board-certified specialty in order to restore the status and numbers of family physicians. The scope of family practice that is envisioned, however, would be so restricted in depth as to raise serious doubts that sufficient medical graduates would be attracted to careers in this new specialty. Better training in broadly-based general or family practice—rather than a specialty board, per se—is the only realistic way to elevate status and attract more medical students to this field.*

Editor's Note: This article on a highly controversial, rapidly changing subject is said to express the viewpoint of the California Academy of General Practice and the large majority of general practitioners in California.

THE CONCEPT OF COMPREHENSIVE medical care, which until now has been known as general practice, is undergoing close study and analysis against the backdrop of socio-economic and technological changes affecting all of medicine. Recent trends and events associated with these studies would indicate that general practice, in its traditionally broadest application, is destined for radical revision under an emerging, altered concept of comprehensive patient care. In fact, the very words that have for many decades identified this kind of over-all care under one physician are about to fall into disuse. Such terms as *first contact physician*, *primary physician*, *personal physician*, and *family physician* are now heard instead of *general practitioner*. Of these terms, *family physician* is the one now most widely used. At its 1966 national meeting, the American Academy of General Practice adopted a resolution recommending a change in name to The American Academy of

Family Physicians. In the recent past, many have proclaimed the imminent demise of the general practitioner, and this action by the Academy sounds the death knell of the old name at least, while ringing in the specialty of family practice.

Whether comprehensive and continuing care based on one physician is labelled family practice or general practice is of no moment. What is *meant* by family practice in the context of the emerging recommendations that envision this branch of medicine as a bona fide, rewarding and attractive specialty is a matter of real concern. For, unless family practice does possess these qualities, it cannot successfully compete with the other branches of medicine. Without them it will fail to draw medical students and graduates into its fold no matter how many board certificates or specialty diplomas may be entailed. It follows that if candidates are not attracted in sufficient numbers to this new specialty, then the new family physician will soon join the old general practitioner in extinction.

Preparations for establishing a Board of Family Practice proceed apace. These preparations are carried forward by a chorus of approbation in

Submitted 10 April 1967.

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which the voice of organized medicine is heard with hardly a discernible note of dissent. The public has also joined in the general acclaim, anticipating that its long unheeded clamor for more family physicians is about to be answered. Suddenly, family practice is to become a high-ranking specialty and is to enjoy equal status in the house of medicine.

The general approval is summarized in the reports recently issued by three separate committees, namely, the Millis Commission (the Citizens' Commission on Graduate Medical Education), the American Academy of General Practice Committee on Requirements for Certification, and the American Medical Association Ad Hoc Committee on Education for Family Practice. These reports are in almost complete agreement on the basic structure projected for the new specialty of family practice. Any assessment of the future of family practice must rest on an examination and interpretation of these reports.

First, let's consider the matter of status. Admittedly, the status of the family physician has fallen as that of the specialist has risen. Medical students have understandably become less and less attracted to careers in family practice. Medicine itself, and hospitals in particular, have joined in this layering of status. Much of the public, too, began to think of the family physician as a second class citizen within the medical community. It is little wonder that medical students gave family practice a wide berth. All three of the reports cited above recognize the importance of this factor when they speak of the equal status that the family physician of the future must have.

How is this high status to be gained? By giving the family physician a board certificate? Obviously, such a certificate is but window dressing. What will the substance behind the certificate be? What will the family physician of the future do? What will he be trained to do? And, perhaps most importantly, what will he be *allowed* to do? For, status in our society is entwined with *doing*.

The three reports are in general agreement that family practice is to be a specialty in breadth rather than depth. Although it is certainly a completely new definition of "specialty," this concept would appear to carry with it an aura of special status. The epithet *breadth* seems innocuous enough at first sight. However, since all the other specialties are specialties in depth, it follows that family practice must stay superficial in all its

breadth if it is to avoid encroachment and conflict *vis-a-vis* its sister specialties. Such superficial participation in medicine, no matter how broad, cannot be broadly rewarding or attractive—if, indeed, it can be called a specialty.

Let us examine the concept of breadth-rather-than-depth against its historical background. Until very recently, every attempt to assemble and launch a Board of Family Practice foundered because it was inevitably on a collision course with already established specialties, notably and most dramatically with that of surgery. However, the conflict exists no less substantially and essentially with such other specialties as obstetrics, orthopedics and internal medicine. Until recently, it was apparent to all who studied the matter that in order for family practice to be presented as a rewarding and attractive career in medicine, it must encroach to some flexible degree of depth upon the other specialties. Without this encroachment, the family physician could not offer the type of comprehensive and continuing care for which there is public clamor. With this encroachment, it appears impossible for a Board of Family Practice to gain the cooperation and approval of the established specialties. This has been the impasse faced by attempts to define an acceptable Board of Family Practice.

How has this impasse now been solved? Very simply, by skirting around it. The previously unsolvable problem has been solved by ignoring it. Briefly, the problem is that there has been an undesirable decline in the numbers and status of family physicians and that a dangerous vacuum has developed in the area of comprehensive and continuing health care. The searched-for solution has been to elevate the status of the family physician, attract a greater number of medical graduates into family practice and thereby eliminate the vacuum.

One of the committees above cited (AAGP Committee on Requirements for Certification) chides those who would persist in pursuing the "impossible" solution—that is, the solution directed toward a Board of Family Practice that would include the right to be involved in any medical discipline for which the family physician is qualified by reason of training, experience and talent. The public, and supposedly the American Academy of General Practice, have been pressing for this level and this concept of comprehensive and continuing care based on a well-trained family physician. The committee finds a "solution"

by abandoning this goal and the need that underlies the problem and then substituting something called "the family physician of the future." Thus, a solution is arrived at by changing the nature of the problem.

All three Committees and their spokesmen, either openly or by inference, envision the family physician of the future as a family counselor, an advisor on environmental medicine, a junior-grade psychiatrist, a practitioner of preventive medicine, a therapist for minor complaints and, finally, a reliable diagnostician capable of recognizing serious illness and knowing what specialist or group of specialists should be called upon for definitive action. Of course, the family physician of the future will be the "captain of the team" and the "coordinator" of the assembled talent. This will be his new and high status as a diplomate of the coming Board of Family Practice. It matters not that the full-fledged general practitioner of today is already doing this and more, yet is presumably lacking in status.

Before embarking on a three- or four-year residency in family practice, the medical graduate will want some answers and some assurances. If the board-certified family physician of the future is qualified by virtue of training and experience to diagnose and repair an inguinal hernia, will his right to perform the indicated operation be respected? If he is equipped by training and experience to diagnose and treat a coronary occlusion, will he be allowed to attend his patient without calling in unnecessary consultation? If a fracture lies within the scope of his training and experience, will the patient be allowed to receive the direct, continuing care of his family physician? These are some of the questions that a potential candidate for a family practice residency must ask. Statements ranging from "the family physician of the future should not expect to do surgery" to "he should be prepared to do 'applicable' surgery" are hardly satisfactory answers. With equal logic, the prospective resident can certainly project the restrictions in surgery to the other specialty fields of medicine. He will probably come to the conclusion that he cannot live by breadth alone and will choose to immerse himself deeply in one of the "real" specialties.

What are the alternatives? First, it would be well to get back on the track of the original problem, which is to really raise the status of the family physician so as to attract greater numbers of medical graduates to careers in family practice.

Basically, the principal factor responsible for the loss in status by the family physician has been his failure to achieve adequate training in relation to the changing medical climate of the last several decades. Approximately 75 per cent of today's general practitioners have not had *any* residency training. This is to say that the preparational background required of the general practitioner has not changed materially in the past 30 to 40 years, a time during which the rest of medicine was imposing ever higher standards of graduate education upon itself. This is the basic reason that the general practitioner has suffered a fall in status in the eyes of his colleagues and his patients—and probably, too, in his own eyes.

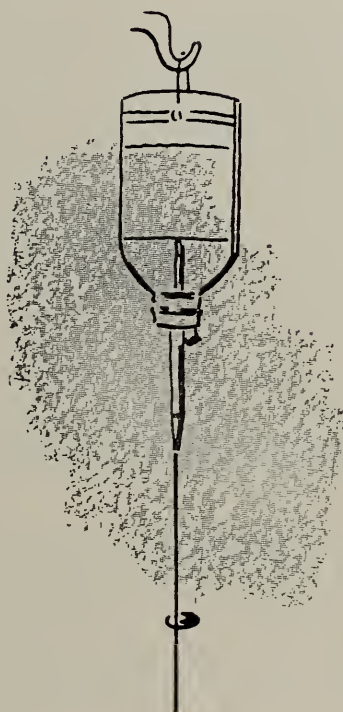
If we grant, in light of the needs of today and of the reasonably foreseeable future, that there does exist a critical necessity for the survival and growth of family practice, the problem is not met by destroying the concept of family practice in order to satisfy the compromises and concessions that would make possible a Board of Family Practice. If family practice is really a desirable and needed thing it will remain so, whether with a board or without. The way to elevate the status of family practice is not through a dilution and weakening of its content but through a real elevation of standards that will justify the vigorous retention of all its traditional content. Whether such elevation includes a formal board is of no intrinsic consequence.

The indicated elevation of standards in family practice must be accomplished in the same manner that it has been achieved in the specialties—through the creation of enough *good* residencies. The California Academy of General Practice, the largest state chapter of the AAGP, has pioneered such residencies on a limited scale. The experience gained and the results of these programs have been reassuring and encouraging. These high-quality residencies attract more candidates than there are posts available. They encompass a high level of training and experience in depth in the disciplines of broadly based family practice. The family physician emerging from a residency program of this type need have no misgivings about status. He possesses the credentials of adequate preparation and the capability of *doing*. These are the keys to status and to self-esteem.

Such high-quality residencies are needed in great numbers and on a national scale if we are to fill the vacuum that has arisen in family practice.

Medical schools and graduate education programs must undergo a reorientation in dominant goals and a repolarization of emphasis in favor of producing more well-trained family physicians. Some specialty fields are already over-crowded. It is probably true that if there were not now a shortage of family physicians, there would now be an oversupply of practically all specialists. Perhaps the field of the specialist should revert to what it was in the beginning—the rare, the unusual, the com-

plicated case. Perhaps the board specialist in obstetrics and gynecology should not be interested in attending the routine pregnancy and delivery. Perhaps this should be the province of the well-trained family physician, who will recognize the rare, the unusual, the complicated, and call in the specialist consultant. An army of well trained family physicians backed up by a select corps of board specialists would appear to answer the clamor against too many generals and too few generalists.



Some Medical Problems of Chronic Hemodialysis

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■ *Chronic intermittent hemodialysis may relieve some medical problems of terminal uremia (for example, azotemia, acidosis, hypertension, neuromuscular disorders, bleeding, pericarditis) to such a degree that many patients are able to resume their normal activity. There remain, however, problems which are not readily changed by hemodialysis (anemia, peripheral neuropathy, pruritus, sexual impotence, renal osteodystrophy). These, together with medical problems possibly caused by hemodialysis (for example, osmotic disequilibrium, errors in dialysate composition, hepatitis, hemosiderosis, isoimmunization from blood transfusions, shunt problems and psychological problems of dependency upon the artificial kidney) represent a limitation of the present type of hemodialysis therapy.*

CHRONIC HEMODIALYSIS is a relatively new technique capable of extending the life of patients who otherwise soon would die of uremia. While the clinical syndrome of chronic uremia is well known, the pathogenesis remains largely a matter of speculation. There is a general overall correlation of the severity of uremic symptoms with the increasing levels of nitrogenous "waste products" such as creatinine and urea, but the specific substances whose retention causes the symptoms and the pathologic changes of uremia are unknown.^{2,6,28,39}

Chronic dialysis induces recurrent temporary remissions in the degree of azotemia, and presumably in the degree of retention of other accumulated toxic products. Such partial or intermittent correction of the chemical abnormalities in the

plasma usually produces striking improvement in uremic symptoms such as nausea and anorexia and serves to encourage the patient facing the initial period of indoctrination and adjustment to the dialysis regimen. Other manifestations of the uremic state are slower to resolve, and ancillary therapeutic measures may be required for their control.

Even optimum therapy does not constitute complete replacement of renal function, since in its present form chronic dialysis is at best only intermittent. The period when the biochemical composition of plasma is most "normal" is restricted to the brief interval shortly after dialysis; thereafter, increasing biochemical uremia is evident until the dialysis procedure is repeated. The degree and duration of "tolerable" degrees of such biochemical uremia are unknown, and despite the most efficient application of intermittent dialysis techniques, there remain a number of unsolved medical problems due to the failure of treatment to correct all the clinical pathologic aberrations that constitute the chronic uremic state. Certain of

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This work was supported in part by U. S. Public Health Service Training Grant No. TI AM 05383 and Contract No. DHEW PH 43-66-1158.

Submitted 7 February 1967.

Reprint requests to: Metabolism Section, Wadsworth V. A. Hospital, Los Angeles 90073 (Dr. Rubini).

these problems may be minimized or possibly avoided by more efficient and more frequent dialysis, but at present they remain a limitation of the application of chronic hemodialysis therapy—that is, medical problems that occur *despite* chronic hemodialysis.

There are also medical problems in chronically dialyzed patients that are *caused* by dialysis. These include certain biochemical complications and acute disturbances in fluid and electrolyte balance that occur because of the dialysis procedure. Technical problems such as cannulation, errors in dialysate composition and mechanical failure of components are included in these acquired medical complications that seem related to the dialysis procedure rather than to chronic uremia.

The purpose of this report is to review the medical experience with chronic dialysis in a group of 24 patients who have received over 280 patient-months of therapy. In this group hemodialysis has been done more than two thousand times. Some additional data are provided by reviewing the pertinent literature.

TABLE 1.—*Medical Problems Which May Be Relieved by Chronic Dialysis*

- 1. Hypertension
- 2. Neuromuscular disorders
- 3. Generalized skin and mucous membrane bleeding
- 4. Pericarditis
- 5. Metastatic calcification (pseudogout)

Medical Problems Which May Be Relieved By Chronic Hemodialysis (Table 1)

The degree of biochemical “success” achieved by chronic dialysis depends to a large measure upon the efficiency of the dialyzer employed and the duration of dialysis.¹¹ Clinical success, on the other hand, depends to variable degrees upon the patient’s capability and willingness to restrict his intake of water, electrolytes, protein and possibly other substances to amounts tolerated in the interval between procedures and removable by dialysis. Medical problems of chronic dialysis encompass both biochemical and clinical failures. The degree of biochemical control achieved by Kiil dialysis twice weekly for 12 to 14 hours is illustrated in Chart 1. Efficiency of the dialysis pro-

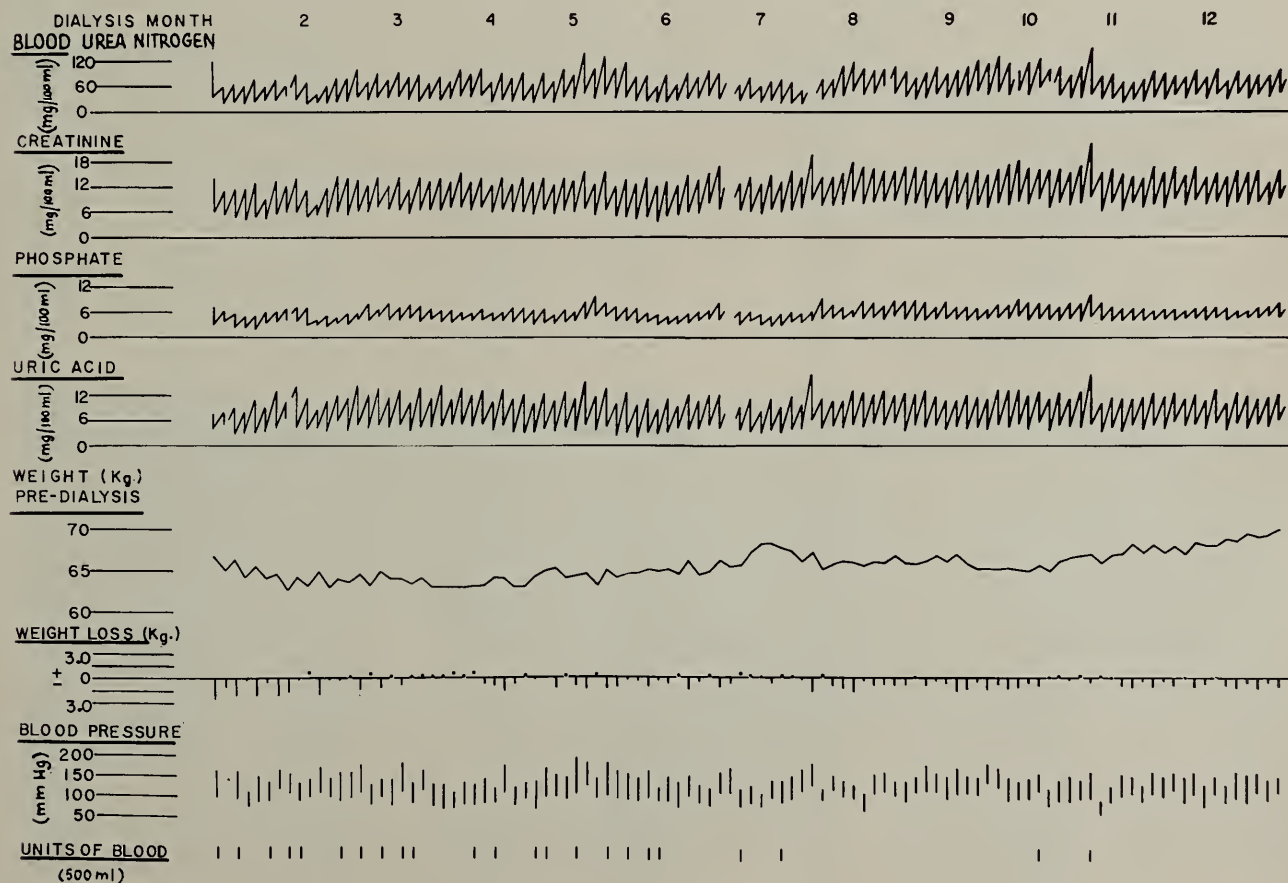


Chart 1.—The first-year biochemical course in a patient now in the 25th month of dialysis. Prescribed diet was 50 gm of protein and 400 mg of sodium. Note the monotonous “saw-toothed” course. The accumulation of uric acid between dialysis procedures is somewhat greater in this patient than in others, but clinical podagra has not developed. An unusual feature in this patient’s course is the diminishing transfusion requirements.

cedure in removal of certain retention substances is presented in Table 2.

Hypertension. Most patients have moderate to severe hypertension and are receiving some anti-hypertensive medication at the time treatment is started. With adequate salt depletion (low-sodium dialysate and dietary salt and fluid restriction) and ultrafiltration, the use of antihypertensive drugs may be diminished or even stopped.^{9,31,33,37} However, a low sodium content of dialysate (120 to 125 mEq per liter) may induce a shift of water from dialysate into the patient, and cerebral edema

and convulsions may occur.^{23,24} To prevent a fluid influx from such hypo-osmolar dialysate, osmotically active substances such as urea or dextrose may be added to the dialysate.¹¹ When ultrafiltration is desired, a positive osmolal gradient may be used in addition to negative pressure gradients across the dialyzer. The response of hypertension to chronic dialysis is presented in Table 3.

Neuromuscular disorders. The acute jactitations and tremulousness observed at the onset of therapy usually disappear after dialysis has been done several times. Unexpected recurrences, however,

TABLE 2.—Chemical Components of Blood Before and After Dialysis

| Component Investigated | Before (mg per 100 ml) | After | Efficiency-Mean* (Per Cent) | Amount Removed (Grams) |
|------------------------|------------------------|----------|-----------------------------|------------------------|
| Urea nitrogen | 80.5±21.9 | 5.9±1.6 | 52.8 | 3.2±1.6 |
| Creatinine | 12.5±2.5 | 29.0±9.1 | 64.0 | 48.0±11.0 |
| Phosphate | 7.2±2.4 | 4.2±1.1 | 41.7 | Not measured |
| Uric acid | 7.9±2.0 | 3.2±0.8 | 59.5 | 2.2±1.2 |

Average blood flow 191±44 ml per min. in 714 dialyses.

*Average of mean values obtained in each of nine patients who had had dialysis from 43 to 134 times.

TABLE 3.—Influence of Chronic Hemodialysis Therapy on Hypertensive Disease Wadsworth Veterans Administration Hospital (As of November 1966)

| Case | Months on Dialysis | | Cardiomegaly (X-ray) | Electrocardiogram | Eye Ground (Keith-Wagner) | Blood Pressure | | Antihypertensive Medication |
|----------|--------------------|-----------------|----------------------|-------------------|---------------------------|----------------|---------|-----------------------------|
| | | | | | | Standing | Supine | |
| 1. | 20 | Before Dialysis | Yes | LVH* | KW II | 160/108 | 184/120 | Yes |
| | | Present | Improved | LVH | KW II | 144/110 | 160/110 | Yes |
| 2. | 32 | Before Dialysis | No | LVH | KW II | 158/110 | 190/110 | Yes |
| | | At Death | Yes | LVH | KW II | 150/90 | 170/100 | Yes |
| 3. | 26 | Before Dialysis | No | WNL† | KW I | 140/94 | 144/74 | No |
| | | Present | Yes | WNL | KW II | 132/94 | 136/88 | No |
| 4. | 26 | Before Dialysis | Yes | WNL | KW I | 114/70 | 184/88 | Yes |
| | | Present | Yes | LVH | KW I | 148/88 | 160/88 | Yes |
| 5. | 11 | Before Dialysis | No | LVH (?) | WNL | 168/110 | 160/100 | Yes |
| | | Present | Yes | LVH | KW I | 120/90 | 130/88 | Yes |
| 6. | 3 | Before Dialysis | Yes | LVH | KW II-III | 140/90 | 160/80 | Yes |
| | | Present | Yes | LVH | KW I | 165/105 | 178/100 | No |
| 7. | 14 | Before Dialysis | No | WNL | KW II | 150/104 | 180/80 | No |
| | | Present | Yes | LVH | KW I | 146/104 | 158/84 | Yes |
| 8. | 13 | Before Dialysis | No | WNL | KW II | 112/84 | 128/92 | Yes |
| | | Present | No | WNL | KW II | 128/92 | 130/90 | Yes |
| 9. | 10 | Before Dialysis | No | R & LVH†† | KW III | 102/80 | 158/104 | Yes |
| | | Present | No | LVH | KW II | 150/110 | 180/120 | Yes |
| 10. | 7 | Before Dialysis | No | WNL | KW III | 130/80 | 86/60 | Yes |
| | | Present | Yes | WNL | KW III | 180/130 | 182/136 | Yes |
| 11. | 17 | Before Dialysis | Yes | LVH | KW II | 150/80 | 140/80 | No |
| | | Present** | Yes | LVH | KW I | 140/76 | 180/70 | No |
| 12. | 24 | Before Dialysis | Yes | LVH | KW III | 140/100 | 180/110 | Yes |
| | | Present | Yes | LVH | KW I | 128/98 | 148/100 | Yes |
| 13. | 8 | Before Dialysis | No | WNL | WNL | 160/90 | 168/82 | No |
| | | Present | No | WNL | WNL | 130/96 | 150/90 | No |
| 14. | 29 | Before Dialysis | Yes | LVH | KW II | 170/110 | 180/114 | Yes |
| | | Present | Yes | LVH | KW I | 130/90 | 140/100 | No |
| 15. | 25 | Before Dialysis | Yes | RBB‡ | KW II | 190/110 | 230/130 | Yes |
| | | At Death | Yes | RBB & LVH | KW II-III | 180/110 | 220/120 | Yes |
| 16. | 18 | Before Dialysis | Yes | WNL | KW I | 170/110 | 240/130 | Yes |
| | | Present | Yes | LAH‡‡ | KW II | 210/120 | 220/126 | Yes |

*Left ventricular hypertrophy; †Within normal limits; ‡Biventricular hypertrophy; **Now 10 months post-transplant; ††Right bundle branch block; ‡‡Left auricular hypertrophy.

may present difficult problems of management. In some patients, increasing the frequency of dialysis has proved helpful. In others, diphenylhydantoin, phenobarbital and atropine-like anti-Parkinsonian agents may be helpful. Some of the neuromuscular abnormalities have been due to drugs, especially the phenothiazine derivatives. In a recent case in our experience, oxycodone seemed to be causative. Although hypocalcemia is evident in most patients with chronic uremia, severe hypocalcemia is infrequent in chronically dialyzed patients; and even in those patients with hypocalcemia and twitching, only rarely has the administration of calcium salts influenced the neuromuscular disorder. Convulsions may occur in patients suffering a crescendo of neuromuscular disturbances or they may occur *de novo*. The possibilities in differential diagnosis of a convulsion in a chronically dialyzed patient are extensive, and careful study is necessary before attributing convulsions to the moderate degree of intermittent uremia present. Uremia potentiates the convulsive action of drugs such as pentylenetetrazol, and it is likely that any other potential convulsion-producing insult to the central nervous system may be more potent in a uremic patient. The effect of dialysis in inducing rapid water shifts into the brain is probably a case in point and will be discussed later.

Uremic bleeding. Nonspecific bleeding tendencies in uremia are more frequently observed in acute renal insufficiency than in chronic uremia. They may be aggravated by total body heparinization during dialysis.^{8,30} Regional heparinization may be employed safely. Bleeding occurring after

the first several weeks of adequate chronic dialysis is usually due to a specific cause—for example, thrombocytopenia, heparin excess or an organic lesion.

Pericarditis. The presence of uremic pericarditis at the beginning of chronic dialysis therapy usually implies that treatment has been delayed too long. With chronic dialysis slow improvement may be anticipated in most cases. Pericarditis may also become evident for the first time in patients who have been chronically dialyzed for many months. With continuing dialysis it may disappear, but gradual tamponade can occur even in well-dialyzed uremic patients.^{3,35} Regional heparinization should be used, lest acute hemorrhagic cardiac tamponade occur with whole body anticoagulation. All uremic patients with radiologically apparent cardiomegaly should be suspected of having a pericardial effusion. Filling of the pericardial sac is usually slow, and symptoms of pericardial effusion may be insidious and consist of fatigue, weakness and bizarre cerebration, rather than the more classic symptoms referable to the precordium. A cardinal manifestation of cardiac tamponade in patients receiving chronic hemodialysis may be a decreasing volume of urine (in those cases in which significant amounts of urine are still produced) well before the development of edema, hypotension and a narrow pulse pressure. Paradoxical pulse has not been commonly found in our experience, and the presence of pain or friction rubs has been variable. Diagnosis is facilitated by newer pericardial scanning techniques, but it can usually be made by careful application

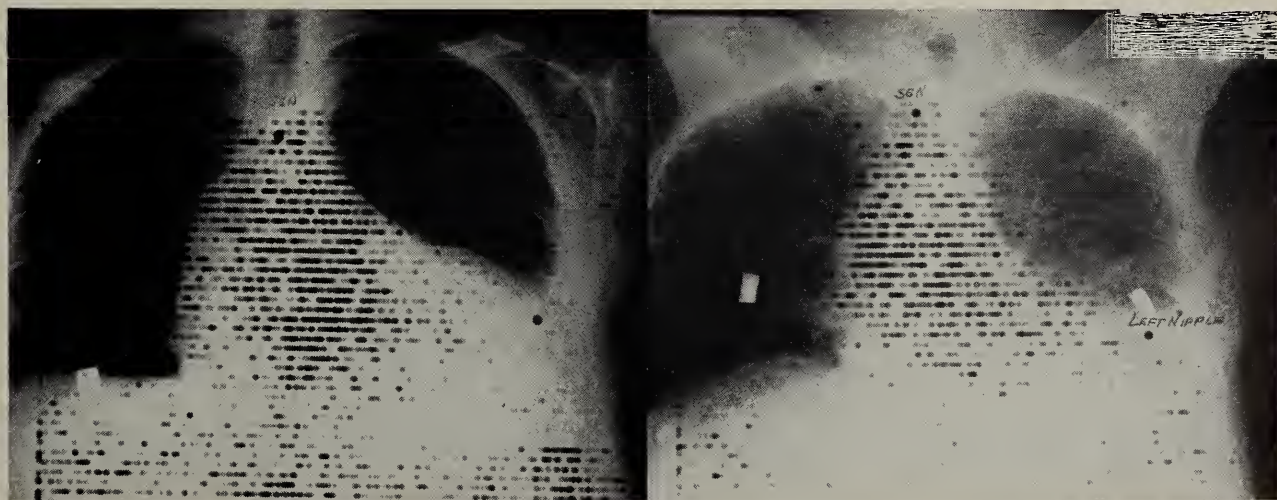


Figure 1.—*Left*, pericardial effusion demonstrated by scanning after I^{131} albumin (aggregate) injection. Progressive oliguria and falling blood pressure developed over the preceding week. Repeated pericardial taps afforded only temporary amelioration of tamponade and a resection of the anterior pericardium was performed. *Right*, pericardial scan one month after operation.

of conventional techniques of physical and radiologic examination. Finite diagnosis is established by aspiration of pericardial fluid. While the onset of pericarditis in a uremic patient is usually considered ominous, the prognosis of uremic pericarditis seems to be improved in patients receiving chronic hemodialysis. In one of our patients pericardiectomy was required because of recurrent hemorrhagic tamponade (Figure 1).

Metastatic calcification seems amenable to treatment by augmenting dialysis time. It is undoubtedly secondary to skeletal disease, and is discussed in the following section. Soft tissue calcification may be aggravated by vitamin D therapy or the use of too much calcium in the dialysate (see additional discussion under "Medical Problems Caused by Dialysis.")

Medical Problems Usually Not Changed by Dialysis (Table 4)

In addition to those complications of chronic uremia which usually respond to chronic dialysis,

TABLE 4.—*Medical Problems Usually Not Changed by Dialysis*

1. Anemia
2. Peripheral neuropathy
3. Skin pigmentation and pruritus
4. Sterility and sexual impotence
5. Renal osteodystrophy
6. Secondary gout

TABLE 5.—*Blood Transfusions for Patients Receiving Chronic Hemodialysis,* Wadsworth Veterans Administration Hospital (As of 15 September 1966)*

| Patient | Months of Treatment | Average Transfusions Per Month† |
|----------|---------------------|---------------------------------|
| 1. | 18 | 0 |
| 2. | 25 | 4 |
| 3. | 25 | 2.3 |
| 4. | 9 | 1.9 |
| 5. | 12 | 2.9 |
| 6. | 11 | 2.9 |
| 7. | 8 | 2 |
| 8. | 5 | 2.5 |
| 9. | 22 | 1.5 |
| 10. | 6 | 0.6 |
| 11. | 16 | 1.3 |
| 12. | 27 | 0 |

*Not included in these data: Patients on chronic hemodialysis program three months or less; patients not now surviving; patients transplanted; patients receiving home-based dialysis.

†Based on most current six-month period.

(Using the listed 12 patients, average transfusions per month per patient are 1.8).

there are several medical problems in which the response to dialysis is less predictable. In some patients partial relief is noted during chronic dialysis, and some investigators attribute this improvement to dialysis. Others remain pessimistic and consider this relationship fortuitous.

Anemia, secondary to uremia, is usually normochromic and normocytic and is usually not relieved by hemodialysis. More frequent hemodialysis, however, may decrease the need for blood transfusions. The exact cause of anemia in chronic renal disease is not entirely understood. Radio-iron turnover studies indicate a bone marrow depression in some instances, and Cr⁵¹ studies suggest a shortened red blood cell survival in others. Erythropoietin studies are not conclusive, but suggest an incomplete inhibition or a partial deficit.^{14,20} After a successful kidney transplant, on the other hand, anemia tends to improve rapidly even in patients who had been maintained on hemodialysis for years. The blood transfusion requirements in our patients are shown in Table 5. Note also the decreasing transfusion requirements in the patient shown in Chart 1.

Peripheral neuropathy is usually manifested in uremic patients by paresthesia and painful, burning sensations in the legs and feet. In some patients loss of deep tendon reflexes and muscle wasting also develop. Some authorities consider these to be separate and distinct clinical syndromes.³¹ Neurologic problems appear in chronically dialyzed patients somewhat more frequently than in those who are not treated, but nerve conduction times in uremic patients who have not been dialyzed generally show some impairment of nerve conduction, suggesting that neuropathy is a part of the uremic syndrome.^{34,37} With adequate hemodialysis, patients with mild sensory or minimal motor neuropathy will often improve and have shortened conduction times.¹⁸ However, in a case in which the neuropathy is extensive, further deterioration occurs sometimes even in the face of adequate hemodialysis. Vitamin administration and physical therapy have not been helpful. Following successful transplantation, the neuropathic symptoms may slowly decrease, and occasionally even pronounced neuropathy may improve.^{17,23}

Finally, certain problems are unchanged by chronic dialysis. These include the skin changes, sterility and sexual impotence, and probably the decreased bone density that is variously ascribed

to secondary hyperparathyroidism, calcium depletion or impaired bone replacement.

Pigmentation of the skin and severe pruritus are common in chronic uremia. Even frequent dialysis does not seem to improve itching in some patients, but such patients are occasionally relieved by antihistaminic agents and the use of skin emollients.²³ In some cases extensive microscopic calcification of the skin is evident on biopsy. Urochrome retention in the skin, causing the typical pigmentation, is little changed with chronic dialysis.

Sterility and sexual impotence are problems in most male patients despite reasonable wellbeing and apparent metabolic equilibrium. Intermittent hemodialysis does not seem to substantially improve this psychologically important symptom. It seems likely that fertility is reduced independent of the generalized problems of impotence. The testicular atrophy and tubular hyalinization reported in chronic uremia are not likely to be improved by chronic dialysis therapy.³⁴ However, we have had one patient after one year of chronic hemodialysis whose wife became pregnant; yet "pater semper incertus."

Uremic or renal osteodystrophy entails complex problems that are beyond the scope of this review. The substantial incidence of gross bone disease in our patients is depicted in Table 6. Calcium content of dialysate should be carefully adjusted to match ultrafilterable calcium in the plasma. Phosphate retention may be reduced by use of

aluminum hydroxide gel, but so far we have not found any therapy that we believe is of consistent benefit. Supplemental calcium and vitamin D may be useful in patients with hypocalcemia, but generally, intestinal absorption of calcium remains decreased in these patients (vitamin D resistance) and vitamin D may actually increase bone reabsorption and cause protracted hypercalcemia without relieving bone pain. The therapeutic possibility of parathyroidectomy is attractive.^{23,34}

"Pseudogout" as well as true secondary gout may occur in chronically dialyzed patients.⁷ Pseudogout is usually due to calcium phosphate deposition in periarticular soft tissue, but occasionally joint cavities and tendon sheaths may be directly involved. The rapidity with which metastatic calcification may grow in a uremic patient is alarming. Figure 2 illustrates dissipation of metastatic calcification with dialysis.

Secondary gout. Uric acid retention is more prominent in some patients than in others and indicates a critical limitation of dialysis technique. The use of allopurinol in patients with colchicine-responsive arthritis is suggested. Prophylactic administration of colchicine may also be useful.

Medical Problems Caused by Dialysis (Table 7)

Two kinds of medical problems may be caused by dialysis. First are the problems that occur during or directly following the dialysis procedure. They include a so-called "disequilibrium syndrome," abnormal plasma composition such as hypokalemia, hypercalcemia, hyperglycemia and

TABLE 6.—Skeletal Changes In Patients Receiving Chronic Hemodialysis (As of 1 November 1966)

| Patient | Hemodialysis Treatment (Months) | Alkaline Phosphatase K.A. Units (Normal 3-13) | Bone X-ray |
|----------|---------------------------------|-----------------------------------------------|--------------------------------------------------------------------------|
| 1. | 20 | 19.0 | Os spine |
| 2. | 32 | 75.0 | Os feet |
| 3. | 26 | 13.0 | Re clavicle, fingers |
| 4. | 26 | 51.0 | Re fingers, F _x ribs |
| 5. | 11 | 10.3 | WNL |
| 6. | 3 | 9.0 | Os spine |
| 7. | 14 | 11.0 | WNL |
| 8. | 13 | 27.0 | WNL |
| 9. | 3 | 22.0 | Arthritis spine |
| 10. | 10 | 12.0 | WNL |
| 11. | 7 | 13.0 | WNL |
| 12. | 24 | 27.0 | Ca hands (soft tissues) F _x T ₆₋₇ , 8th ri. rib |
| 13. | 8 | 14.0 | WNL |
| 14. | 18 | 33.0 | Os spine |
| 15. | 29 | 12.0 | F _x L ₁ Re cysts—long bones |

Os=Osteoporosis; F_x=Fracture; Ca=Calcifications; Re=Resorption; WNL=Within normal limits.



Figure 2.—*Left*, the readily palpable tender mass over the left lateral buttock gradually became painless and smaller and finally disappeared over a period of several months of intensive chronic dialysis. *Right*, patient had Ca^{47} kinetic studies compatible with severe hyperparathyroidism. Diagnosis of extensive cystic disease involving liver and kidney was established on exploration and biopsy.

alkalosis; acute cardiovascular problems such as hypovolemic shock, acute hypertension and pulmonary embolization (due to either clots or air); and miscellany such as pyrogen reactions and aberrant drug response. Chronic problems include the risk of serum hepatitis; various hematologic problems including iron overload; shunt

problems such as infection, thrombosis, hemorrhage; personality problems and even psychosis.

Acute Problems Caused by Dialysis

Disequilibrium syndrome. The so-called “disequilibrium syndrome” is associated with rapid biochemical correction of severe uremia. Dialysis lowers urea concentrations more rapidly in the extracellular than in the intracellular compartment of the body. This results in an osmotic gradient across the cell membrane and draws fluid into cells, leading to cellular and, particularly, cerebral edema. The syndrome occurs mostly in the early weeks of the dialysis treatment when blood urea is highest, but may recur even after many months of dialysis if the patient increases his protein intake. Severe headache, vomiting, hypertension and even convulsions and coma may develop. Increased intra-ocular and cerebrospinal fluid pressure, and electroencephalographic changes during or shortly after hemodialysis, represent objective measures of this water shift.^{24,28} To minimize the risk of cerebral edema, especially in the first few times dialysis is carried out, it may be

TABLE 7.—*Medical Problems Which May Be Caused by Chronic Dialysis*

- | | |
|----|----------------------------------------------------------------------------------------------|
| A. | Acute intermittent problems |
| 1. | Disequilibrium syndrome |
| 2. | Abnormalities of plasma composition: hypokalemia, hypercalcemia, hyperglycemia and alkalosis |
| 3. | Cardiovascular problems: hypovolemic shock, acute hypertension and pulmonary embolization |
| 4. | Miscellaneous: pyrogen reactions, aberrant drug response |
| B. | Chronic problems |
| 1. | Hepatitis |
| 2. | Hematologic problems: cytopenia, iron overload and heparin |
| 3. | Shunt problems: infection, thrombosis, hemorrhage |
| 4. | Personality disorders—psychoses |

necessary to add an osmotically active substance such as urea, glucose, fructose or mannitol to the extracellular fluid in order to minimize the osmotic disequilibrium. This may be accomplished by infusion into the patient, or more simply by addition to the dialysate. Uremia itself may alter the barrier between blood and spinal fluid and may contribute to the cause of this syndrome.

Dietary restriction of potassium is difficult in the chronically dialyzed patient, and hence removal of potassium must depend on a gradient between plasma and dialysate. The most dangerous aspect of acute potassium removal is the sudden precipitation of *arrhythmias*, especially in digitalized patients. This is further accentuated by the simultaneous correction of hypocalcemia, hyponatremia and acidosis that occurs with dialysis. Severe hyperkalemia is rare in chronic dialysis patients except in instances of rapid catabolism, hemolysis or severe acidosis. Most authorities recommend that digitalis should be avoided insofar as possible in chronically dialyzed patients. If digitalization is deemed absolutely necessary, electrocardiographic monitoring is advisable during dialysis, and judicious increase in the concentration of potassium in the dialysate may minimize the potassium gradient and hence the rate of change in the plasma. Repeated dialysis with low dialysate potassium levels may cause chronic *potassium depletion*.

Hypercalcemia. A peculiar syndrome of severe vomiting and headache was described recently and is called the "hard-water syndrome." It is caused by high levels of calcium and magnesium in tap water used for dialysate preparation, usually when a failure in the water-softening system occurs.¹² In four patients we have observed peptic ulcer disease which seemed related to excess calcium in the dialysate.³⁸

When large amounts of glucose are added to the dialysate in order to increase fluid loss or to compensate for a low-sodium dialysate, *hyperglycemia* with cellular dehydration similar to that of diabetic acidosis may develop in patients who have a disturbance in carbohydrate metabolism (a defect of uremia in some patients). These cases are fortunately rare.³²

Although acute changes in acid-base relationship in the extracellular fluid are prominent during acute dialysis, changes are usually minor in patients receiving chronic dialysis because the degree of hydrogen ion retention between treatments

is minimal. Pre-dialysis values are shown in Table 8. With the dialysis procedure there is a gradual overcompensation toward metabolic alkalosis. In addition, continued overventilation may superimpose a respiratory alkalosis which reaches a peak 12 hours after dialysis.

Hyperosmolar dialysate and negative pressure can produce excessive *volume depletion*. This may result in severe hypotension and shock. It is less common in pumpless hemodialysis systems, or when the artificial kidney is primed with fluid or blood before it is attached to the patient. Conversely, in certain cases hemodialysis may cause a progressive rise in the blood pressure during the procedure. The reason for this phenomenon is unknown; a possible role of the aldosterone-renin system activated by the blood volume decrease is suggested.^{22,27}

Miscellany. In some instances recurrent obscure fever has developed during dialysis. The possibility of a *pyrogen* in either dialysate or transfused blood is difficult to rule out. The use of buffy coat free blood may be helpful.²⁹ Chronic dialysis patients may tolerate *drugs* erratically because most water-soluble materials not tightly bound to tissues or circulating plasma proteins may pass through the dialyzer membrane. Alternatively, the uremic state may modify drug metabolism or response. Therefore, adjustment in dosage is needed with dialyzable drugs. On the other hand, caution must be observed in the use of poorly dialyzed drugs normally excreted by the

TABLE 8.—*Acid-base Studies Immediately Before Chronic Dialysis*

| | |
|------------------------------------------------|-------------------------------|
| Number of patients studied | 17 |
| Total number of dialysis procedures | 1191 |
| Mean per patient | 70 |
| Range in number per patient | 9 to 176 |
| pH mean* ± mean SD* | 7.36 ± .05 |
| Range of coefficient of variation† | 0.2 per cent to 1.8 per cent |
| Carbon dioxide pressure mean* ± mean SD* | 41.4 mm Hg ± 4.16 |
| Range of coefficient of variation† | 2.8 per cent to 21.6 per cent |
| Bicarbonate mean* ± mean SD* | 23.0 mEq/L ± 2.24 |
| Range of coefficient of variation† | 2.1 per cent to 37.7 per cent |
| "Buffer base" mean* ± mean SD* | 28.2 mEq/L ± 3.93 |
| Range of coefficient of variation† | 3.7 per cent to 15.2 per cent |

*Obtained by averaging the individual mean and standard deviation (SD) of each patient.

SD
† ——— determined in each patient.
Mean

kidney. Severe toxicity or serious side effects may occur.^{10,25,28}

Chronic Problems Caused by Dialysis

Serum hepatitis is a feared complication of frequent blood transfusions. Recently in England and Sweden epidemics of severe hepatitis with several deaths occurred among patients and staff members.¹³ Epidemiologic evidence suggests a virulent form of infectious hepatitis rather than a blood contamination. How effectively present methods used to sterilize the dialyzer destroy hepatitis virus is uncertain.

Hematologic problems represent a broad spectrum. Besides the constant anemia of uremia, the reported complications range from minor hemolytic reactions due to the development of antibodies induced by frequent blood transfusions, to grave allergic phenomena. Leukocyte and *platelet antibodies* may lead to *pancytopenia*.³⁴ Such cytopenia may be accentuated by the adherence of white cells and platelets to the dialysis membrane.^{1,21,28} *Hemosiderosis* may be anticipated in patients on chronic hemodialysis requiring frequent transfusions. Blood iron saturation is elevated in most of the chronic dialysis patients, and internal organs are loaded with iron-containing pigment (Figure 3). The amount of iron derived from dialysate tap water is negligible in comparison with the amount of iron administered via blood transfusions (Table 9). Chelating agents may prove useful in reducing the accumulation of iron and possibly of other trace metals.^{15,40}

Heparin, used in large amounts in chronic hemodialysis, may enhance the risk of bleeding, particularly in patients with peptic ulcer disease or pericarditis. This can be minimized by careful control of clotting times, and by the technique of regional heparinization using protamine as a hepa-

TABLE 9.—*The Transfer of Iron During Hemodialysis*

- A. Whole body's uptake of the iron added to dialysate delivered during 12 hours of dialysis
 Average* 0.20 per cent
 Range 0.08 to 1.00 per cent
- B. Iron saturation and concurrent approximate iron load from transfusions per month, from dialysate containing 10 µg per 100 ml

| Iron Saturation (Per Cent) | From Blood (mg Per Month) | From Dialysate (mg Per Month) |
|-------------------------------|------------------------------|----------------------------------|
| Average† 48.7 | Average† 727.3 | Average† 26.5 |
| Range 23 to 77 | Range 500 to 1200 | Range 20 to 32 |

*Nine patients; †11 patients.

TABLE 10.—*Data on Cannula Placements in Patients Receiving Chronic Hemodialysis, Wadsworth Veterans Administration Hospital (As of 15 September 1966)*

| | |
|----------------------------------|-------------------------------|
| In 269 patient-months* | |
| 18 Patients | |
| 21 Arterial cannula replacements | |
| 27 Venous cannula replacements | |
| Longest cannula survival | |
| Arterial | 18 months |
| Venous | 21 months (still functioning) |
| Average cannula survival | |
| Arterial | 12.80 months |
| Venous | 9.96 months |

*Patients in chronic hemodialysis program three months or less are not included in these data.

rin antagonist. Even then, however, a rebound effect can occur because protamine is more rapidly metabolized than heparin.⁴ Chronic heparin administration has been reported to interfere with bone structure and may cause atrophy of the adrenal cortex.^{16,19,26,41}

The maintenance of chronic access to the circulation remains a major problem of chronic dialysis (Table 10). *Arteriovenous shunt* has been kept functioning adequately for many months and even years.³¹ However, the presence of an intravascular prosthetic device is responsible for a variety of complications in chronic dialysis patients. The most common is *infection*. Initially such infections are usually restricted to the entrance or exit sites of the skin surface, but they may extend to deeper tissues and compromise the shunt or even induce *septicemia*. Most of these infections are due to *Staphylococcus aureus*, coagulase-positive. Prompt and proper antibiotic therapy is mandatory. In our experience, vancomycin has been most effective. Another problem of maintaining the arteriovenous shunt is *clotting*. Early recognition of clotting is necessary if the declotting procedure is to be effective. The declotting carries a risk of infection and a possibility of pulmonary embolism because declotting of the venous cannula may involve pushing of the clot into the venous circulation. Infected emboli may travel through the lungs, causing abscess formation. Every shunt is a potential source of lethal hemorrhage, as the blood flow in the shunt is between 200 and 300 ml per minute. Leakage or disruption may cause severe blood loss after fresh shunt implantation. Oozing at one or both cannulation incisions occurs frequently the first few times dialysis is carried out but it is rarely sig-

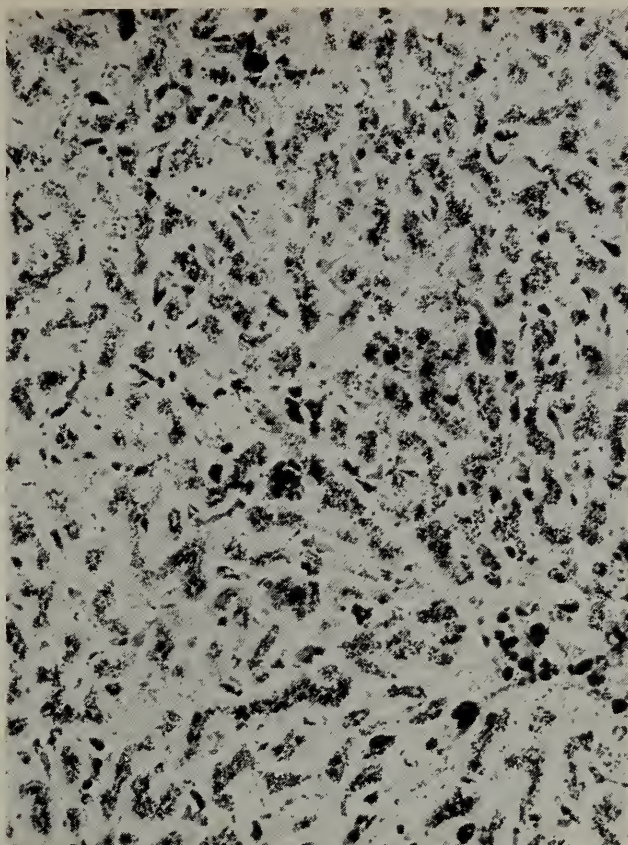


Figure 3.—Liver specimen stained for iron with Prussian blue ($\times 40$). Note accumulation in both parenchymal and Kupffer cells and fine granular appearance of deposits. Duration of dialysis 20 months. Liver function tests indicated normal SGOT and SGPT and normal albumin globulin content.

nificant and usually can be controlled by local pressure. Occasionally surgical hemostasis is required, and sometimes oozing is serious enough to warrant regional heparinization. Fibrin formation around the cannulated vessel usually stops the oozing in several weeks.²⁴

Psychological and psychiatric problems are of importance in many chronically dialyzed patients. The dependence of patients on the "kidney machine" presents a complicated and stressful relationship, especially in unstable or immature patients. Dialysis often interferes seriously with the self-sufficiency and self-confidence of the patient. A whole scale of *psychotic reactions* may arise, from simple anxiety to severe depressions, which may lead to suicidal attempts. Recent interest in developing more self-reliance on the part of the patient may minimize these complications.^{33,36}

Discussion

The success of chronic dialysis therapy depends to some degree on the selection of patients whose

uremia has not been so severe and protracted as to cause irreparable damage to vital organ systems. Premature initiation of therapy with its restrictive regimen is equally undesirable, but the optimum criteria for case selection remain unresolved. Most of our patients selected for dialysis were seriously ill; all were symptomatic to the degree that they were partially or fully incapacitated. The state of the patient at the time of selection substantially influences the incidence and degree of medical problems of chronic dialysis and hence it is difficult to compare results from one center to another.

Although intermittent dialysis is no longer considered an experimental procedure, it is still a relatively new means of treatment and in its present form does not represent complete treatment for chronic renal disease. Short of successful kidney transplantation, a fully mechanized and automatic, highly efficient, small artificial kidney which could be carried and would function continuously, remains the aim of chronic dialysis treatment.⁵ In the meanwhile, intelligently directed dialysis offers the otherwise terminal uremic patient opportunity for protracted survival with reasonable health. The fact that some serious medical problems remain unsolved by chronic dialysis should be understood by both patient and physician.

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Acute Myocardial Infarction in Los Angeles County

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INTEREST IN THE MANAGEMENT of acute myocardial infarction has sharply increased as a result of the advocacy of special care units by individual investigators and various governmental and voluntary agencies.¹ To appraise the potential impact of such programs on the care of acute myocardial infarction in Los Angeles County, a survey was made of the usual records of individual hospitals to determine the current status of coronary heart disease management. It should be noted that the more difficult job of testing the accuracy of these records by observation of patients was not attempted as a part of this survey. A secondary goal was to find out how much interest there is in the establishment of coronary care units and nurse training.

Questionnaires were mailed to the hospital administrators as well as to the chiefs of the medical services of all hospitals of record in the county. The replies were separated into three groups based on the number of beds in the responding hospital. The best response was from hospitals of over 95 beds. Forty-seven in that group responded, and 38 of them gave complete answers to all questions. Several that did not give complete answers explained that their records were not adequate for the information requested.

Acute coronary insufficiency was included in the questionnaire for completeness and for accuracy checks.

Results of the survey are summarized in Table 1.

Several points are of interest. Some hospitals have a much higher incidence of acute coronary insufficiency as a discharge diagnosis and as a cause of death than might be expected. In some hospitals the total number of patients treated for either acute infarction or coronary insufficiency had an interesting relationship to the total number of beds. Similarly, mortality rates varied considerably from hospital to hospital. The Los Angeles County Hospital reflected the higher mortality rate usual in large public institutions.²

DEFINITIONS

CORONARY CARE UNIT. A special care area in a hospital with specially trained personnel (registered nurses) which admits only patients with actual or suspected acute myocardial infarction. Such areas have electrocardiogram monitoring devices and ancillary resuscitation equipment. Ideally there is a central nursing station with private or semi-private rooms.

INTENSIVE CARE UNIT. A special care area in a hospital for acutely ill patients. Such units may be entirely for medical or entirely for surgical patients, or for a mixture of both. They usually have resuscitation equipment; there may or may not be monitoring devices and specially trained personnel, such as registered nurses.

Submitted 10 March 1967

Reprint requests to: Coronary Care Unit, Los Angeles General Hospital, 1200 North State Street, Los Angeles 90033

TABLE 1.—Data From Myocardial Infarction Survey—Hospitals of 95 or More Beds in Los Angeles County

CODE:

AI=Acute infarction (definite or probable); ACI=Acute coronary insufficiency; ICU=Intensive care unit; CCU=Coronary care unit.

*Indicates desire of hospital to have assistance of a knowledgeable physician in planning a coronary care unit.

? Indicates equivocal answer.

— Indicates no answer.

| Hospital | No. of Beds | Data on Infarction and Coronary Insufficiency | | | | Data on Special Care Units | | | |
|------------------------------------------------|----------------|--------------------------------------------------|-----------------------|------------------|-------------------------|----------------------------|------------|------------------|------------------------|
| | | Condition | Total Cases | Deaths | Mortality (Per Cent) | Beds In ICU | Has CCU | Planning CCU? | Wish M.D. Help?* |
| Los Angeles County Hospital | 3,522 | AI ACI Total | 1,487 140 1,627 | 691 23 714 | 46.4 16.4 43.9 | 12 | No | Yes | Yes |
| Wadsworth Gen. Med. & Surg. Hosp. | 1,025 | AI Total | 411 411 | 151 151 | 36.7 | 0 | No | Yes | Yes |
| Olive View Hospital | 1,006 | AI ACI Total | 36 67 103 | 26 28 54 | 52.4 | 1 | No | Yes | No |
| Veterans' Admin. Hosp. (Sepulveda) | 970 | AI ACI Total | 113 247 360 | 42 26 68 | 18.8 | 0 | No | Yes | Yes |
| St. Francis Hosp. of Lynwood..... | 530 | AI ACI Total | 240 284 524 | 60 12 72 | 13.5 | 10 | No | Yes | No |
| Veterans' Admin. Hosp. (San Fernando) | 519 | AI ACI Total | 44 7 51 | 16 0 16 | 31.4 | 1 | No | Yes | Yes |
| Cedars of Lebanon Hosp. | 504 | AI ACI Total | 150 306 456 | 27 48 75 | 16.4 | 8 | Yes | Yes | No |
| Good Samaritan | 431 | AI ACI Total | 242 1 243 | 68 1 69 | 28.9 | 14 | No | Yes | No |
| St. Mary's Long Beach Hospital..... | 380 | AI ACI Total | 255 199 454 | 61 4 65 | 14.3 | 10 | No | Yes | Yes |
| St. Joseph's Hosp. | 371 | AI ACI Total | 215 138 353 | 56 5 61 | 17.3 | 9 | No | Yes | Yes |
| Huntington Memorial Hosp. | 343 | AI ACI Total | 26 56 82 | 9 5 14 | 17.1 | 12 | No | No | Yes |
| St. Vincent | 300 | AI ACI Total | 109 98 207 | 32 9 41 | 19.8 | 0 | No | Yes | Yes |
| Pomona Valley Comm. Hosp. | 296 | AI ACI Total | 15 157 172 | 4 43 47 | 27.3 | 8 | No | No | Yes |
| Presbyterian Inter-Community Hospital | 280 | AI ACI Total | 189 75 264 | 12 7 19 | 7.2 | 8 | No | No | Yes |
| White Memorial Hosp. | 279 | AI ACI Total | 120 — 120 | 43 — 43 | 35.0 | 6 | No | Yes | Yes |
| St. John's Hospital | 265 | AI ACI Total | 162 155 317 | 38 16 54 | 17.0 | 7 | No | Yes | Yes |
| California Hospital | 256 | AI ACI Total | 173 85 258 | 68 6 74 | 28.7 | 5 | No | Yes | No |
| Presbyterian Olmstead Memorial Clinic | 236 | AI ACI Total | 51 12 63 | 26 0 26 | 41.3 | 4 | No | Yes | Yes |
| U.C.L.A. Medical Center | 250 | AI ACI Total | 133 329 462 | 45 71 116 | 25.1 | 4 | No | Yes | ? |
| Inter-Community Hosp. (Covina) | 229 | AI ACI Total | 183 87 270 | 26 4 30 | 11.1 | 8 | No | Yes | Yes |

TABLE 1.—Data From Myocardial Infarction Survey—Hospitals of 95 or More Beds in Los Angeles County (Cont.)

| Hospital | No. of Beds | Data on Infarction and Coronary Insufficiency | | | | Data on Special Care Units | | | |
|------------------------------------|----------------|--------------------------------------------------|-------------------|------------------|-------------------------|----------------------------|------------|------------------|------------------------|
| | | Condition | Total Cases | Deaths | Mortality (Per Cent) | Beds In ICU | Has CCU | Planning CCU? | Wish M.D. Help?* |
| Freeman Memorial Hosp. | 225 | AI ACI Total | 416 171 587 | 61 20 81 | 13.8 | 4 | Yes | No | No |
| San Pedro Community Hosp. | 185 | AI ACI Total | 110 — 110 | 38 — 38 | 35.5 | 4 | Yes | — | No |
| Methodist Hosp. So. Calif. | 184 | AI ACI Total | 139 71 210 | 52 1 53 | 25.2 | 7 | No | Yes | Yes |
| St. Luke Hospital | 170 | AI ACI Total | 136 6 142 | 29 1 30 | 21.1 | 4 | No | Yes | Yes |
| Valley Presbyterian Hosp. | 162 | AI ACI Total | 97 101 198 | 23 4 27 | 13.6 | 4 | No | Yes | Yes |
| Santa Teresita Hosp. | 156 | AI ACI Total | 65 22 87 | 22 0 22 | 25.3 | 7 | No | ? | ? |
| Queen of the Valley Hosp. | 152 | AI ACI Total | 60 50 110 | 8 1 9 | 21.1 | 1 | No | Yes | Yes |
| West Valley Comm. Hosp. | 152 | AI ACI Total | 9 117 126 | 2 10 12 | 9.5 | 3 | No | Yes | Yes |
| Centinella Valley Comm. Hosp. | 150 | AI ACI Total | 308 38 346 | 189 29 218 | 63.0 | 6 | No | No | ? |
| Antelope Valley Hosp. | 149 | AI ACI Total | 31 58 89 | 3 9 12 | 13.5 | 6 | No | No | Yes |
| Little Company Mary Hosp. | 143 | AI ACI Total | 134 55 189 | 18 4 22 | 11.6 | 4 | Yes | No | Yes |
| Comm. Hosp. of San Gabriel | 141 | AI ACI Total | 23 45 68 | 6 1 7 | 10.3 | 4 | No | Yes | Yes |
| Temple Hospital | 141 | AI ACI Total | 39 123 162 | 12 4 16 | 9.8 | 0 | No | No | Yes |
| Beverly Comm. Hosp. | 137 | AI ACI Total | 90 — 90 | 17 — 17 | 16.7 | 2 | No | No | Yes |
| Morningside Hosp. | 136 | AI ACI Total | 198 — 198 | 41 — 41 | 20.7 | 0 | No | No | Yes |
| Santa Clarita Hosp. | 124 | AI ACI Total | 21 3 24 | 4 1 5 | 20.8 | 0 | No | Yes | Yes |
| Dominguez Valley Hosp. | 100 | AI ACI Total | 35 55 90 | 5 2 7 | 7.8 | 12 | No | Yes | Yes |
| La Mirada Comm. Hosp. | 99 | AI ACI Total | 22 12 34 | 10 — 10 | 29.1 | 0 | No | Yes | Yes |
| Valley Doctors Hosp. | 99 | AI ACI Total | 44 42 86 | 4 1 5 | 5.8 | 0 | No | Yes | Yes |
| Childrens Hospital | 241 | AI ACI Total | 0 — 0 | 0 — 0 | — | 0 | No | No | No |
| Totals | 15,038 | Total | 9,743 | 2,441 | — | 195 | 4 | 27 | 28 |

Incomplete Data

| Hospital | Data on Infarction and Coronary Insufficiency | | | | | Data on Special Care Units | | | |
|----------------------------------|-----------------------------------------------|-----------|-------------|--------|----------------------|----------------------------|---------|---------------|------------------|
| | No. of Beds | Condition | Total Cases | Deaths | Mortality (Per Cent) | Beds In ICU | Has CCU | Planning CCU? | Wish M.D. Help?* |
| Glendale Sanitarium & Hosp. | 380 | | 215 | — | — | 6 | No | Yes | Yes |
| Hollywood Community Hosp. | 99 | AI | — | 8 | | | | | |
| | | ACI | — | — | | | | | |
| | | Total | — | 8 | — | 1 | No | Yes | No |

This survey suggests the need for better standardization of criteria for diagnosis and a concerted effort to improve record-keeping in some hospitals if the effect of efforts to improve survival rates of patients with acute myocardial infarction is to be properly assessed.

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Hematologic Abnormalities And Pesticides

Mortality Rates from Blood Dyscrasia in an Area of High Pesticide Use Compared with Rates in California as a Whole

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■ *In recent years, concern has been expressed that a positive relationship exists between certain blood dyscrasias and long-term exposure to pesticides. A search and analysis of death records in Kern County and in California as a whole failed to reveal such a relationship.*

RECENTLY, INFORMAL COMMUNICATIONS, published and unpublished manuscripts^{4,6} and personal interviews in the local press by scientists have implied that the apparent increase in cancers of the blood and blood-forming organs are a direct result of pesticide residues in our food and environment.

This concern over the increasing use of pesticides has led in recent years to a searching appraisal of our knowledge of the effects of "long-term" exposures which in turn produce delayed effects upon human health. The 1964 report of the California Governor's Committee on Pesticide Review said that "... there ought to be established a program to acquire reliable information on the amount and severity of human illness resulting from exposure to pesticides."

There is an extensive body of information on the acute effects of the commonly used pesticides.

From the California Pesticides Study, State of California Department of Public Health, Berkeley.

Submitted 19 January 1967.

Reprint requests to: Community Studies on Pesticides, State Department of Public Health, 2151 Berkeley Way, Berkeley 94704 (Mr. Mengle).

This investigation was supported by Contract PH 86-65-87 from the Department of Health, Education and Welfare, U.S. Public Health Service, Office of Pesticides, Atlanta, Georgia.

DDT = 1,1,1-trichloro-2, 2-bis = (*p*-chlorophenyl) ethane

tepp = tetraethyl pyrophosphate

EPN = 0-ethyl 0-*p*-nitrophenyl phenylphosphonothioate

Systox = demeton

Isopestox = *N,N*-Diisopropylphosphorodiamidic fluoride

Dipterex = trichlorfon

As the use of pesticides in agriculture continues, knowledge of safeguards is refined. Although many cases of poisoning occur, most deaths or serious acute effects can be traced to violations of recommended practices.

Far less is known about the significance of long-term exposure. As West⁹ pointed out, it seems most useful to think of exposure to anything as either acute or long-term and to consider effect as either immediate or delayed. Cutaneous allergic reaction due to long-term exposure to malathion⁸ and bone marrow damage with pancytopenia as-

sociated with long exposure to lindane have been described.¹ In both instances it was immediate effects of long-term exposure that were reported. Practically nothing is known of the delayed effects in man of long-term exposure to pesticides. Neoplasms of mice have been ascribed to long-term exposure to dieldrin and aldrin²; decreased viability of pheasant offspring has been attributed to DDT⁵ and decreased productivity of certain white pelican colonies due to toxaphene.⁷

In 1965, the California State Department of Public Health entered into a contract with the Federal Government to undertake an intensive study of health effects of pesticides in Kern County, California. Kern County, with a population in 1966 of 333,000 persons, has been a principal agricultural area since the late nineteenth century. At present \$350,000,000 in agricultural sales each year make it the third richest agricultural county in California and in the United States. With the increase of planting and harvesting has come the associated technological use of machines and chemicals. Historically, the available chemical materials included the arsenicals, lime-sulphur, petroleum oils and nicotine. During the interval between World Wars I and II, the fluorine compounds were added to the inorganics, pyrethrum and rotenone were added to the botanicals, and synthetic organic materials such as the dinitro compounds and thiocyanates made their appearance.

The compound DDT, developed during World War II for military use mostly, was first used, in limited amount, in Kern County in 1945 but was not in wide use until 1947. Other chlorinated hydrocarbon insecticides—toxaphene, chlordane, aldrin and dieldrin—were introduced into the county in the late 1940's. Meanwhile, research in fungicides produced the dithiocarbamate ferbam

in 1931, and then its disodium salt nabam and its zinc salt zineb in 1943. Maneb, a bisdithiocarbamate, was introduced in 1950.

German work during World War II produced the organic phosphates, among them tepp and parathion. Publication of this work in 1947 led to the commercial development in the United States of additional compounds including: Methyl parathion, malathion, EPN, systox, isopetox, diazinon, and dipterex. All of these materials came on the market between 1949 and 1955 and were used (and many still are used) extensively in Kern County, California. The carbamate insecticides, introduced about 1958, are the last major group to be introduced. During the years 1964 and 1965, the Kern County Agricultural Commissioner reported the use of 145 different pesticidal active ingredients.³

Objective and Method

The objective of this study was to attempt to discover if any important differences exist in death rates from certain specific diseases in Kern County as compared with the State of California as a whole. Ideally, one would like to contrast the pre-World War II rates with the post-World War II

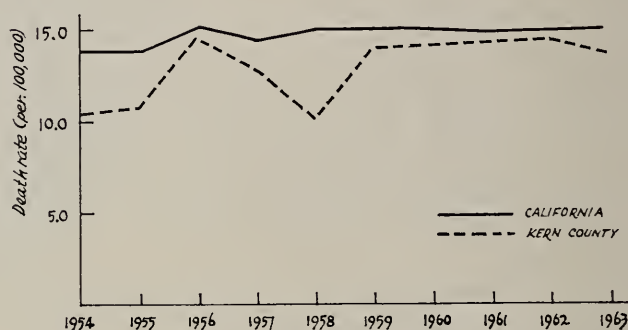


Chart 1.—California compared with Kern County death rates for selected causes 1954-1963 (I.C.D. Nos. 200, 205 and 292.4).

TABLE 1.—Deaths Due to Neoplasms of Lymphatic and Hemotopoietic Tissues and Aplastic Anemia* by Age, Kern County, 1954-1963

| Age (years) | 1954 | 1955 | 1956 | 1957 | 1958 | 1959 | 1960 | 1961 | 1962 | 1963 |
|-------------------|------|------|------|------|------|------|------|------|------|------|
| Less than 5 | 4 | 1 | 1 | 2 | 1 | 2 | 0 | 5 | 2 | 0 |
| 5-14..... | 0 | 0 | 1 | 2 | 0 | 2 | 2 | 2 | 1 | 2 |
| 15-24..... | 4 | 2 | 1 | 0 | 0 | 2 | 4 | 1 | 3 | 2 |
| 25-34..... | 1 | 0 | 0 | 2 | 3 | 3 | 0 | 2 | 3 | 1 |
| 35-44..... | 1 | 6 | 3 | 3 | 0 | 2 | 5 | 1 | 2 | 2 |
| 45-54..... | 1 | 3 | 4 | 1 | 4 | 7 | 3 | 6 | 3 | 4 |
| 55-64..... | 3 | 7 | 7 | 12 | 6 | 9 | 11 | 6 | 5 | 7 |
| 65+..... | 10 | 6 | 13 | 8 | 9 | 9 | 11 | 15 | 19 | 16 |
| Total all ages | 24 | 25 | 30 | 30 | 23 | 36 | 36 | 38 | 38 | 34 |

*International Classification of Disease Codes 200-205 and 292.4, 7th Revision, International Classification of Disease.

TABLE 2.—Deaths Due to Lymphatic and Hematopoietic Disease and Aplastic Anemia* by Selected Groups.
Kern County, 1954-1963

| Group | 1954 | 1955 | 1956 | 1957 | 1958 | 1959 | 1960 | 1961 | 1962 | 1963 |
|-------------------|------|------|------|------|------|------|------|------|------|------|
| Agricultural | 1 | 5 | 2 | 8 | 2 | 7 | 3 | 3 | 3 | 5 |
| Nonagricultural | 18 | 19 | 26 | 18 | 20 | 25 | 31 | 28 | 31 | 27 |
| Occupation | | | | | | | | | | |
| Unknown | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| Under 15 years. | 4 | 1 | 2 | 4 | 1 | 4 | 2 | 7 | 3 | 2 |
| Total | 24 | 25 | 30 | 30 | 23 | 36 | 36 | 38 | 38 | 34 |

*International Classification of Disease Codes 200-205 and 292.4, 7th Revision, International Classification of Disease.

rates, since the "newer" synthetic chemicals were introduced during the post-World War II period. This proved impossible, however, because of the numerous revisions in the international classification of diseases and changes in diagnostic methods.

The diseases chosen for study were neoplasms of lymphatic and hematopoietic tissues (international classification of causes of death numbers 200-205) and aplastic anemia. The number of deaths due to these causes is given in Table 1 by year and age group, and in Table 2 by occupation. The Kern County death rates in Chart 1 were age-adjusted by the direct method.

Results

The results are summarized in Chart 1 which compares California's statewide death rates with the age-adjusted rates for Kern County, California. As can be seen, Kern County follows roughly the same trend and is always lower than the statewide rate. The only noticeable change in the ten-year period seems to be that since 1959, Kern County's death rates for the causes of death under consideration more closely approximate the statewide total, although even this may be fortuitous.

The only conclusion that the investigators can reach is that the chance of death from the reported

causes under consideration in this study are certainly no greater in an agricultural community subject to large annual inputs of agricultural chemicals than they would be on the average throughout the state.

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Carotid Artery Occlusive Disease

Clinical Considerations in Surgical Revascularization

JOHN A. TOLLEY, III, M.D., *Los Angeles*

■ *In clinical evaluation and analysis of 85 consecutive carotid endarterectomies in 74 consecutive patients, the operation was shown to be an effective and safe method of treating cerebral vascular insufficiency. It must be properly timed and performed, and excellent results may be expected, particularly in comparison with nonoperatively treated patients with the same disease.*

ONLY RECENTLY HAS there been a basis for comparison of operative and non-operative treatment of carotid artery occlusive disease at the bifurcation. The basis was supplied in a study by Shenkin and coworkers⁶ of 30 nonsurgical patients, with diagnosis confirmed by arteriograms, who were observed for an average of two years. In 11 of them the condition was improved; in seven it was unchanged or worse; and 12 patients died as a result of stroke in the follow-up period. These results were discouraging in comparison with reports of surgical results in which mortality varied from 3 to 5 per cent.³ Indeed, mortality has been reported as low as 1 to 2 per cent in patients operated upon for symptoms of transient cerebral ischemia or in whom the neurological deficit was stable.^{2,7}

In the present study, mortality was within an acceptable range. Over all it was less than 5 per cent (four deaths in 85 cases); and when operations on patients with acute, frank stroke are excluded the mortality was 2.5 per cent. We have long since given up prompt operation in this latter group because of the obviously forbidding mortality of operating during acute stroke. Two of five patients with such operations in this series died,

and this experience is similar to that of other investigators, who reported hemorrhage or massive edema into the freshly infarcted area occurring frequently.^{4,5,8,9} In the present series one of each phenomenon occurred. Now a delay of at least a month before operation is the present rule in dealing with acute stroke.

It is of particular importance that the advantages of surgical treatment of carotid occlusive disease be reported since it offers 80 to 90 per cent good to excellent results, depending upon the series. This is in sharp contrast to the prognosis with nonsurgical treatment of this disease: 40 per cent of patients dead at two years and up to 80 per cent by the end of the fifth year. It should be added that the vast majority of these patients die of cerebral vascular insufficiency.

Since 60 to 85 per cent of the patients with an acute frank stroke will give a history indicative of previous transient cerebral vascular insufficiency, and since 50 per cent of those with transient ischemia will ultimately have a stroke, there can be no question that strokes are being prevented by revascularization during the transient phase of this disease.^{1,7} Furthermore, investigators generally agree that only an extremely small number of patients will have further cerebral vascular insufficiency after revascularization, and in most cases when they do have insufficiency it is because

From the Department of Surgery, Ross-Loos Clinic, Los Angeles. Submitted 20 March 1967.

Reprint requests to: Ross-Loos Medical Group, 947 West 8th Street, Los Angeles 90017.

they have an uncorrected lesion on the opposite side. The latter is often a factor when improvement postoperatively is less than satisfactory, thus stressing the need for an evaluation of both sides at the time of the examinations for revascularization are being carried out.

The clinical material consists of 85 consecutive carotid endarterectomy operations in 74 patients. All lesions were confirmed at operation after having been diagnosed clinically either by the presence of a bruit reaching a maximal point over the carotid bifurcation, or by angiography. In no case was there false positive diagnosis based on the presence of a bruit. Indeed, bruit was uniformly indicative of a high-grade lesion, although many such lesions did not produce a bruit. Angiography remains the main diagnostic tool (Figures 1 through 5). For the most part it is performed by the injection of contrast media into the aortic arch. In the present series a retrograde (transfemoral) approach to the arch was used in most cases. A transaxillary approach was used when peripheral atherosclerotic disease precluded the femoral approach. Because of the greater risk associated with direct carotid puncture, we used it only when neither of the other approaches was feasible. With correct positioning, pressure injection of sodium iothalamate (Conray®-400) into the aortic arch

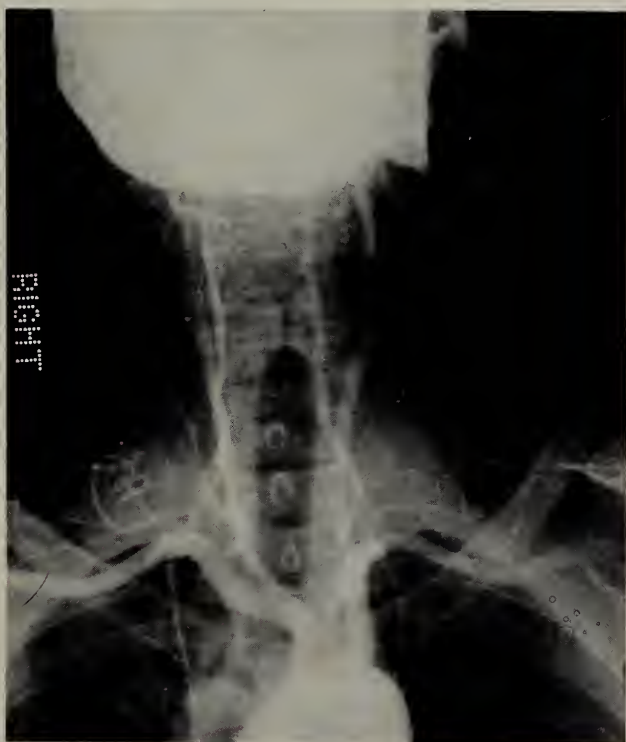


Figure 1.—Arch study showing bilateral internal carotid occlusive disease, and left vertebral artery stenosis at its origin.



Figure 2.—Direct carotid puncture arteriogram showing severe stenosis at the carotid bifurcation, extending into the internal carotid artery. Arteriotomy had to be carried into the internal carotid artery, with subsequent patch grafting.

will visualize both extracranial carotid systems, usually simultaneously, with essentially no risk. Furthermore, since it causes only slight discomfort when local anesthesia is used, examination need not be hurried. Hydration beforehand prevents renal sequelae.

The clinical diagnosis was made by the presence of an audible bruit or angiographically visible defect with associated symptoms. In cases in which diagnosis was based on the presence of a bruit, if the patient did not improve as expected after operation, angiographic examination of the opposite side was carried out. This usually demonstrated the remaining lesion. Also when diagnosis was made by bruit and there was neurological defect on the side opposite the one which would be expected to be involved (so-called "paradoxical deficit") angiography was promptly carried out. In eight such patients the signs were found to be truly paradoxical, as was confirmed preoperatively by angiograms and by prompt resolution of symptoms after operation. From this it appears that patients with paradoxical signs have as good a prognosis for improvement by surgical operation as do patients in whom signs follow the expected pattern. In three patients paradoxical lesions were

suspected, diagnosed and treated successfully after the first operation did not bring about improvement. Eight other patients had similar lesions with orthodox signs, symptoms and resolution following operation, for a total incidence of 13 per cent in this series. Figure 1 is an angiogram made in one such case.

An unexpected finding was the reversibility of static neurological defects residual from stroke that had occurred as much as six years previously. In general, the longer the duration of such defects and the greater the severity, the slower the clinical improvement after operation. However, there were several striking exceptions. In two cases aphasia and hemiparesis of two and four years' duration abated rapidly, and in another case hemiplegia of two years' standing was almost completely resolved.

Like other investigators,⁴ we have repeatedly observed worsening of a stable neurological situation when angiography is done too soon after stroke. Hence we withhold the procedure at this critical time lest it cause complete occlusion of the internal carotid.

Our mortality experience has improved considerably since we have been eschewing operation and even angiography of the aortic arch for at least a month and preferably longer after frank stroke. Mortality and morbidity have further de-



Figure 3.—Severe internal carotid occlusive disease at the carotid bifurcation.

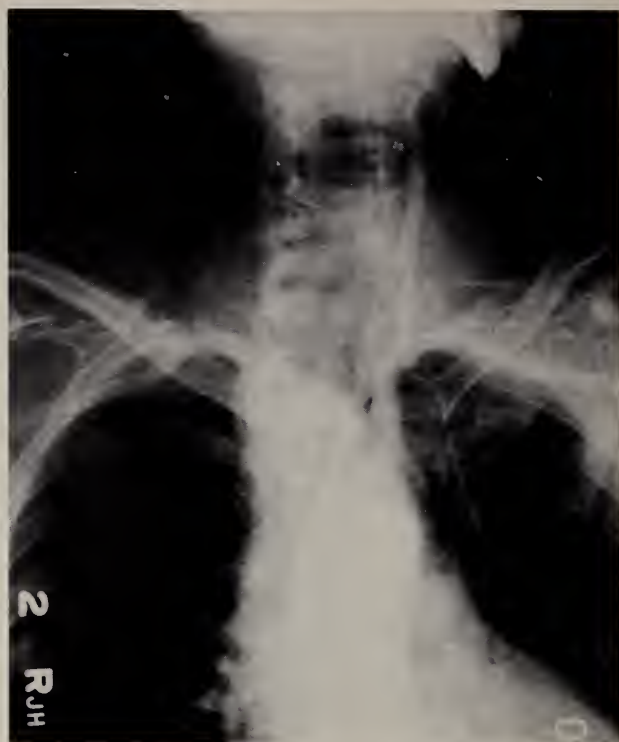


Figure 4.—Severe stenosis of the bifurcation of the left common carotid artery.

clined since we began using hypothermia rather than shunts for the interim protection of patients who cannot tolerate a trial occlusion of the carotid bifurcation.

Operation to determine whether or not the patient can tolerate carotid cross-clamping can be done quite satisfactorily with local anesthesia and only 50 mg of hydroxyzine hydrochloride (Vistaril®) intramuscularly as sedation. Patients who cannot cooperate or are unwilling to do so (usually due to confusion secondary to cerebral vascular insufficiency) are operated upon under general anesthesia with hypothermia. Operation under local anesthesia has permitted extending the benefits to many patients in whom we would be reluctant to use deep anesthesia and hypothermia. For example, several patients in the ninth decade of life underwent operation and none required cerebral protection during cross-clamping.

At this point an important occurrence in one case in the present series should be mentioned: In that case occlusion of the common carotid, which up to this point had been the usual practice in determining tolerance to occlusion, was easily tolerated, the patient remaining alert and able to move all extremities, with no weakness of grip or of plantar flexion, for over five minutes of occlusion. However, when occluding clamps were



Figure 5.—Complete stenosis of the internal carotid artery with retrograde filling. Note catheter introduced into the innominate artery due to insufficient visualization on arch injection.

applied to the external and internal carotid as well as the common carotid, the patient promptly lapsed into unconsciousness and consciousness did not return on release of only the clamps on the internal and external carotid. Thus, it may be presumed that retrograde flow down the external and up the internal carotid was the protective mechanism. Occlusion of the common carotid by external pressure on the neck for whatever purpose, including priming of the patient for occlusion at operation, would be misleading in such cases.

Of primary concern when determining the ability of patients to withstand occlusion is the maintenance of adequate collateral diffusion through the circle of Willis by sustaining the systemic blood pressure at least at preoperative resting levels. The mean resting blood pressure for these patients was 160/90 mm of mercury and pressure was maintained at least at that level by the intravenous infusion of vasopressors during occlusion. Despite recent assertions to the contrary, we continue to give this measure prime consideration. We have often seen the level of consciousness or strength of grip deteriorate concurrent with a decrease in blood pressure, and then return to nor-

mal when hypotension is corrected by infusion of a vasopressor agent.

The operation is depicted in Figures 6 and 7. Arteriotomy is done in the carotid bulb only, thus avoiding the necessity of patch grafting. The procedure is after the method of Wylie and coworkers.⁸ The occluding plaque almost invariably breaks off at normal intima distally. Since it is adherent there is no need to suture the distal intima. In only one case in this series did the disease extend for more than 1.5 cm up the internal carotid (Figure 2). In that case arteriotomy was extended into the internal carotid and patch grafting was carried out later. In view of this possibility, the arteriotomy should be angled toward the internal carotid.

The only other technical aspect not evident, and which facilitates the procedure, is ligation and division of the superior thyroid artery and the ascending pharyngeal artery. The latter, in particular, may not be evident and causes annoying back-bleeding during dissection as it commonly arises from the very bifurcation itself. Infiltration of this area before dissection is important, as the carotid body lies in this location and reflex hypotension may follow manipulation of it.

The only consistent morbidity in this series was headache, usually beginning two to three hours after operation and lasting 36 to 72 hours, then rapid abatement with no treatment except analgesia. It is due no doubt to transient cerebral edema, resulting from the brief period of ischemia at the time of cross-clamping during operation. Occlusion lasted only an average of slightly over seven minutes. Recently the problem has been almost completely averted by parenteral administration of 16 mg of dexamethazone, half of it before operation and half after.

Comment

Of great clinical importance is the fact that vertebral lesions were found to be invariably associated with carotid bifurcation lesions and any vertebral-basilar symptoms were uniformly corrected by carotid endarterectomy. Furthermore, vertebral-basilar symptoms were among the most common, vertigo being the most frequently noted. It responded well to carotid endarterectomy. Contrary to clinical impression in the past, only 40 per cent of the patients with transient cerebral vascular insufficiency proved to have correctible intracranial carotid occlusive disease when investigated by arteriography.

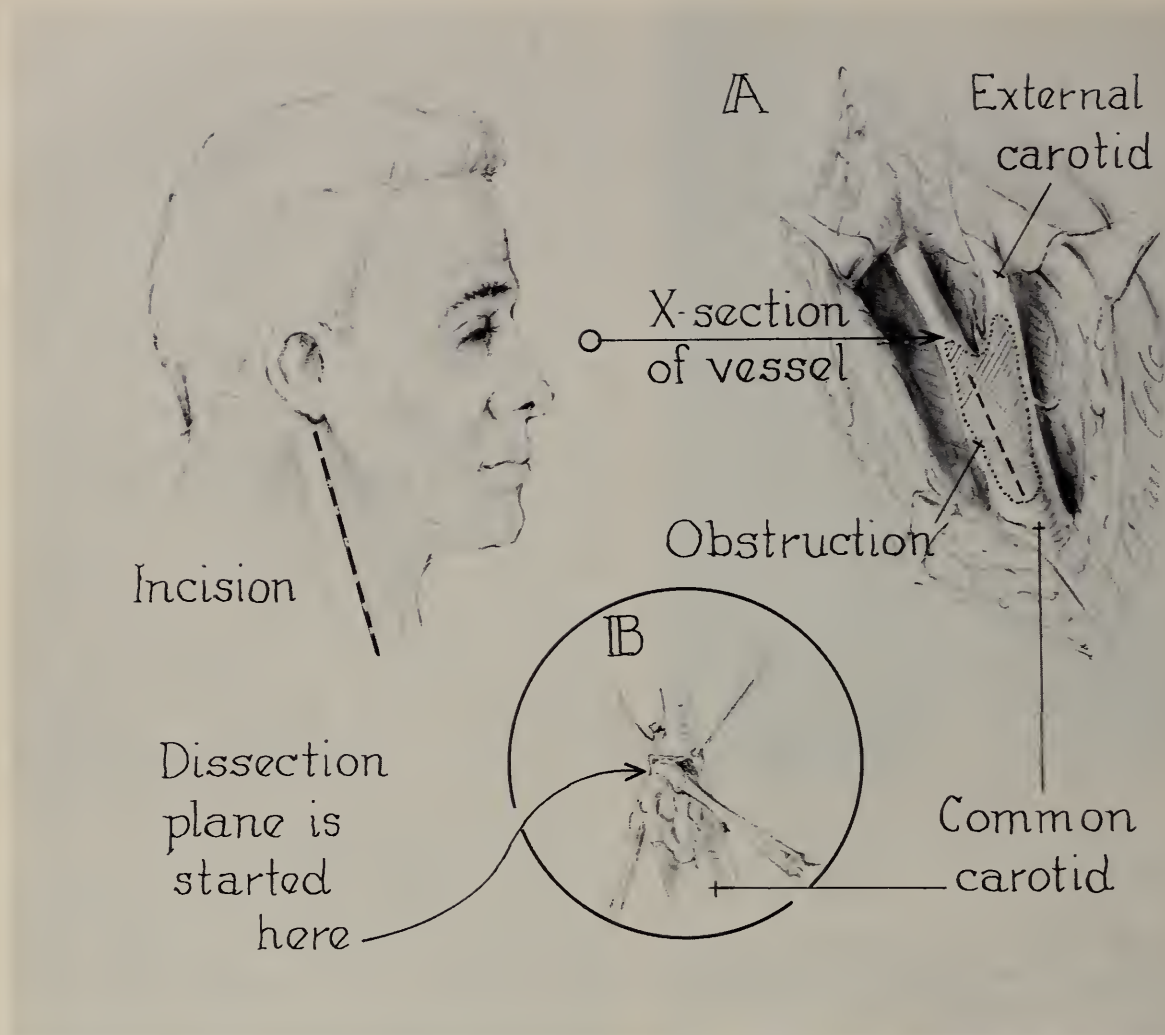


Figure 6.—A—Arteriotomy in the carotid bulb angled toward the internal carotid artery. The shaded area illustrates the usual configuration of the occluding lesion. B—Note the ascending pharyngeal artery ligated. Subintimal dissection is begun.

After vertigo, the next most common symptom was episodic syncope, the episodes becoming more frequent as time passed. Ataxia and hemiparesis were the next most common, followed by aphasia and defects in cerebation. Tinnitus due to the hemodynamic effect of the stenotic arterial lesion *per se*, was very common. It always abated upon removal of the clamps after endarterectomy.

It is pertinent that we consider here four patients, in whom the diagnosis of occlusive disease at the carotid bifurcation was proved by arteriogram, and who refused operation. Closely controlled anticoagulation was chosen as an alternate method of treatment by each patient's private physician. In all cases the symptoms which the patients had when first observed—namely, syncope and hemiparesis in two and vertigo in two—continued or recurred. The intensity and frequency of

symptoms rapidly progressed in all patients. Acute frank stroke, manifested by complete hemiplegia and aphasia, occurred in one patient eight months from the time diagnosis was made and treatment begun. All patients requested operation sooner or later after the time of diagnosis—the interval varying from nine to twelve months. In contrast to anticoagulant therapy, carotid endarterectomy relieved symptoms completely in three patients and resulted in pronounced improvement in the patient with hemiplegia and aphasia.

One patient described a growing intensity of tinnitus due to hemodynamic defect which was evidenced by an increasingly audible bruit. Thus it is evident that anticoagulants in no way influenced the course of this disease in this group of carefully controlled patients. All patients were seen three times weekly, and the prothrombin con-

centration at no time was permitted to rise to more than 20 per cent of normal. A fifth patient in this group, in whom diagnosis was confirmed, died of acute post-traumatic subdural hematoma. Prothrombin time was 10 per cent of normal in this patient at the time of admission one hour after trauma.

Another interesting phenomenon encountered in this series is the concurrence of arterial hypertension with carotid occlusive disease. Eighty-five per cent of the patients had diastolic blood pressure of over 110 mm of mercury when first observed. By the time they arrived at the operating room, after a period of sedation, bed rest and premedication with intramuscular hydroxyzine hydrochloride (Vistaril®), the mean diastolic pressure had been reduced to 90 mm of mercury. The systolic mean dropped from 200 on admission to a range of between 150 and 160 mm. In 90 per

cent of these patients, the mean diastolic pressure stabilized in a range between 70 and 80 mm post-operatively. It is postulated that the gradient proximal to the carotid sinus led to this increase in arterial pressure. In four patients, with otherwise nearly complete relief of symptoms, the pressure did not change until the lesion on the opposite side was corrected.

Our high mortality rate associated with revascularization after acute strokes—two of five patients died—was similar to rates reported by Wyllie^{8,9} (42 per cent), by Perdue⁴ (33.3 per cent) and by Robinson⁵ (21 per cent).

Our series of patients may be roughly divided into two groups, half having had completed stroke presenting with varying degrees of chronic cerebral ischemia, and half having symptoms of transient cerebral ischemia. The results were equally good in both groups—almost 90 per cent of the

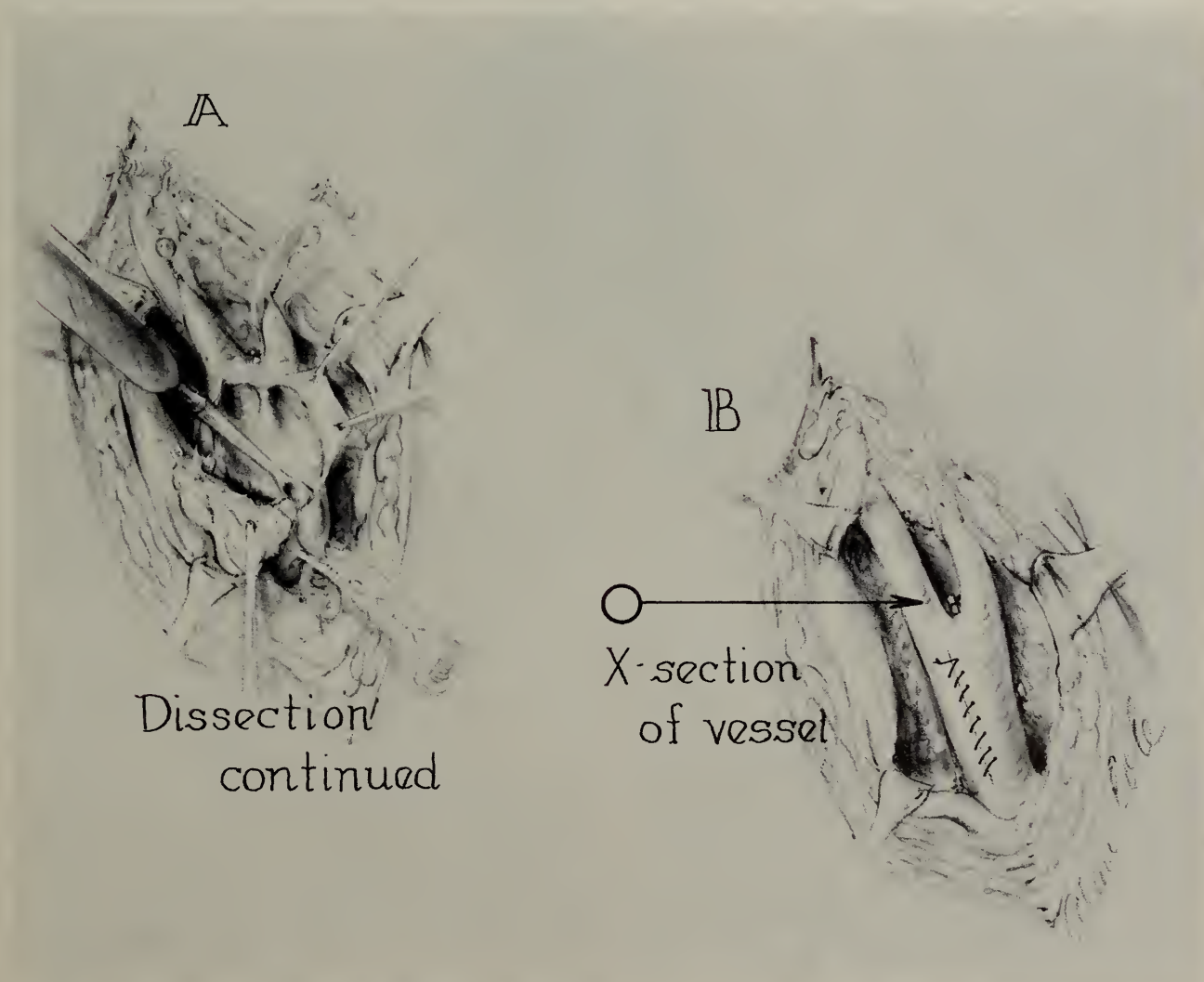


Figure 7.—A—Subintimal dissection completed. B—Closure of arteriotomy without stenosis.

patients having resolution of the chief deficit or symptom complex. These statistics compare favorably with those reported by other investigators.

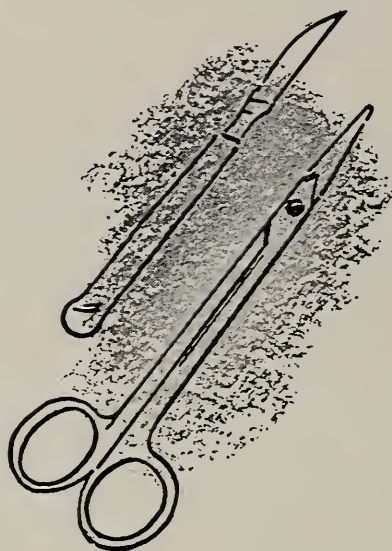
GENERIC AND TRADE NAMES OF DRUGS

Sodium iothalamate—*Conray*®-400

Hydroxyzine hydrochloride—*Vistaril*®

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The Incidence of Major Arterial Laceration Accompanying Fractures of Long Bones

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HEMORRHAGE BEING ASSOCIATED with all fractures, orthopedic surgeons are accustomed to dealing with extremities in which this problem is one of several varieties of tissue reaction to trauma, but there can be wide variation in the degree of significance of the vascular injury.

Up to the end of World War II, major vascular laceration accompanying fractures of long bones was usually dealt with by ligation. Since that time successful methods of repairing vascular injuries have been available. Most recorded observations pertaining to vascular trauma and its management contain an index of the frequency of fracture accompanying vascular injury. Hughes and co-workers¹ reviewed material of this nature from the Korean War and found that of the total number of vascular injuries of all kinds, the variation of incidence of vascular injury associated with fractures in the total group of vascular injuries was from 15 to 56 per cent. Morris and coworkers², in a recent series of 220 vascular injuries in civilians, reported that 25 were associated with fracture or dislocation, an incidence of close to 10 per cent. In neither series was the frequency of vascular injury accompanying fracture assayed.

At the San Francisco General Hospital, we have reviewed the cases of major vascular injury requiring repair associated with fracture from 1957 to 1966. At that time the hospital drew its patients from the indigent population of the City and County of San Francisco. During that period eight-

een thousand fractures were treated, about equally divided between in-patients and out-patients. In all, there were nine cases in which major arterial damage was a concomitant of long bone fracture. The most common site of such concurrence was the femoral shaft. There were four such cases in a total of 333 femoral shaft fractures. During the same period there was one instance of major vascular damage in 144 humeral shaft fractures, one in 261 fractures of the surgical neck of the humerus, one in 72 elbow dislocations, and two in 315 fractures at the proximal tibial level.

This group of vascular injuries does not include traumatic amputations or patients with arteriosclerotic occlusive disease complicating fractures but without laceration. In addition, undoubtedly there were patients with major compound fractures with extensive soft tissue destruction and significant vascular injuries that were not repaired because surrounding soft-tissue damage was too great. The number of such cases is not known, however.

In reviewing this selected group of cases, it was apparent that they were only distinguished from rather routine fracture management problems by the vascular injury. The most interesting observation was a significant delay in diagnosis in two closed fracture cases and in one case of compound fracture. In one of the closed fracture cases the patient was a 65-year-old man with a displaced proximal humeral fracture adjacent to which a false aneurysm appeared six weeks following injury. There was no loss of peripheral pulses and no circulatory embarrassment distally. In the case

Submitted 24 October 1966.

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in which there was a delay of diagnosis associated with compound injury, the patient was a 24-year-old man with a compound femoral fracture from a gunshot wound. Peripheral pulses were present until sudden massive hemorrhage ten days after the injury called attention to major vascular laceration. In two additional instances, major vascular damage was not immediately apparent but recognized within a few hours after the initial treatment of the fracture.

In eight cases surgical exposure was carried out when the diagnosis was established, and in seven of them the laceration was successfully repaired. In the eighth case the arterial defect consisted of an avulsion of all three branches at the popliteal bifurcation level and repair was not technically possible. Below-knee amputation was necessary.

Surgical exposure was withheld in one case in which a laceration of the profunda femoris artery was demonstrated by arteriography and sudden hemorrhage occurred two weeks after injury while the patient was being treated in traction. Peripheral pulses continued, however, and since local skin

contamination added to the risk, operative exposure was not carried out.

Discussion

In this series, the incidence of major vascular injury accompanying long bone fracture was in the vicinity of one per cent when correlated with similar, noncomplicated fractures at the same level. Injury of this type occurred approximately once in every two thousand fractures of all varieties.

Since vascular injury may not be readily apparent on physical examination, arteriography should be utilized in any case where integrity of the circulation is in question. The presence or absence of the peripheral pulses should be recorded on the initial examination of all injuries to extremities and should be determined again at appropriate intervals.

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Brief Psychotherapy: Current Status

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■ *In the past decade, stimulated by public concern with issues of mental health, there has been a new spurt of interest in techniques of brief treatment with circumscribed goals. These are applicable to groups as well as to the single patient. There are still differences of opinion about the effectiveness of brief psychotherapy, particularly the lastingness and depth of the results obtained, yet it is often highly beneficial, especially to previously well-functioning individuals who are involved in a situational crisis. Although probably the best results of brief psychotherapy are with disturbances of moderate severity and recent onset, in practice, it is often tried with a wide spectrum of patients. Brief psychotherapy aims at relief of the patient's major current conflicts rather than at change of his personality structure, which generally requires long-term treatment. Brief psychotherapy is of special relevance for the general physician because the patients whom he sees in large numbers are precisely those best suited for this form of treatment.*

IN THE EARLY 1880's when Anna O., Josef Breuer's patient, referred to her treatment as "the talking cure,"⁵ she was giving a patient's view of a new medical discovery. This new method, which Sigmund Freud then developed into a complex instrument he called psychoanalysis, proved to be the foundation of modern psychotherapy. In its essentials, the new method was quite simple. The patient was encouraged to *talk* to his doctor as freely as possible. In the privacy of the relationship, as the patient recalled *with feeling* the events associated with the onset of his symptoms, the symptoms subsided and disappeared. Time and experience showed that, unfortunately, it was not always possible to limit oneself to this simple scheme. Some symptoms were particularly diffi-

cult and stubborn and did not melt away as easily as those of hysteria. In addition, the patient usually was handicapped not only by his symptoms but by his personality, which often showed serious warpings and interfered with his capacity to manage in life and to participate in the treatment. His past influenced the way he dealt with the present and, in particular, with the doctor. All this needed to be taken into account and treatment in many instances then became much longer. As psychoanalysis developed, its practitioners became less and less content with the simple removal of symptoms and they began addressing themselves to the much more demanding and critical task of ameliorating long-standing personality distortions. As the decades passed the psychotherapeutic setting became increasingly complex and varied. By the 1960's, psychotherapy was no longer restricted to a situation in which the patient, *alone*, talks with his physician. Patients today speak with therapists

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Submitted 10 March 1967.

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under a variety of conditions, in groups as well as singly. Groups may consist of people who share a common relationship (e.g., a family in "family therapy"), a common symptom (e.g., alcoholism), a common diagnosis (e.g., schizophrenia), a common social misadventure (e.g., unwed motherhood), a common interest (e.g., sensitivity training), or simply human suffering in its many and diverse forms. The therapists patients talk with are not always physicians; often they are representatives of other disciplines, and occasionally they are lay persons. The place where the treatment is carried out may be a private office, a clinic, a clubhouse, a church or a television studio. The treatment itself may be long or short, with modest or far-reaching goals, and based on a variety of theoretical points of view. Recently, moreover, fringe "happenings," such as the 30-hour talk marathons and other phenomena which abound in group suggestion, also have appeared on the local scene.¹⁰

In sum, brief psychotherapy, to which this paper is restricted, is only one segment of the currently available treatment approaches. If Anna O. were to seek help today she might wonder *which* talking cure was really for her, and it would be impossible to give her a simple or unqualified answer. One must emphasize the enormous complexity of the field and that divergence of views and methods, rather than consensus, typically is found. For the reviewer this means some difficulty presenting the differences without reference to his personal bias.

The significance of brief psychotherapy is not only a medical but a social one, and derives from the need, apparent to all, to make available to the general public effective remedies for emotional illness. Brief psychotherapy is not new, but in the last few years, under the press of public demand, interest in this form of treatment has grown enormously and with it an impetus to find techniques that are both effective and economical. This interest has expressed itself in a renewed commitment to research in psychotherapy and in a true outpouring of books and articles on this subject. Their number is such that only a few will specifically be mentioned here.

How much brief psychotherapy can contribute to the practical solutions that currently are searched for is unknown, but the predominant feeling in this country is that its potential as a therapeutic tool is considerable. Brief psychotherapy, by itself, cannot make up for the shortage of

trained personnel and, as will be noted more extensively later, is not suitable indiscriminately for all kinds of psychiatric problems. We already know a good deal about the workings of brief psychotherapy, yet more detailed information is needed on many facets. It is hoped that the current search will teach us more accurately the tolerances of this form of treatment—in short, what it can do and what it cannot do—and enable us to make a prescription with greater assurance of precision and effectiveness.

What Is Brief Psychotherapy?

"Brief psychotherapy" immediately seems to define itself in terms of its duration and by an implied contrast with something else, to be called "long-term treatment," which, in turn, consists of approaches of varying length, depth and intensity. Yet, this, without further explanation, does not tell how brief is brief and how long is long.

Traditionally, brief psychotherapy has referred to the one-to-one encounter between patient and therapist, an encounter which purposely has been limited as to over-all duration, scope and goals to be met. In some instances, however, group therapy and family group therapy should be included in the general rubric of "brief therapy" since they may involve only a few sessions. Experiences with *brief* group psychotherapy, while generally described as positive,^{12,23} are still rather incomplete and preliminary and for this reason will not be pursued further here.

An approach to brief psychotherapy that is now in vogue is "crisis therapy."^{4,17} Crisis here refers to the relationship between the patient's distress and his external situation which he perceives as hazardous. Treatment is primarily an effort at helping the patient master the crisis. Probably the chief contribution of the crisis approach is its sharp and highly focused emphasis on the here-and-now: By stressing the *current* disruption in the patient's interpersonal relationships, it helps to define what inner needs have gone unmet as a result of the change in his external circumstances. Also it capitalizes on the observation that patients are more accessible to psychotherapy during states of emergency than at other times. In these ways it enhances the potential for a rapid appraisal and resolution of the patient's difficulty. On the other hand, the concept of crisis lacks clarity since it is used, often interchangeably with "stress," to denote three different sets of phenomena: (1) The stressful event or situation, (2) the state of the

individual who responds to the stressful event (e.g., feelings or symptoms of stress), (3) the stressful stimulus, the individual's reaction to it and the events to which it leads.¹⁸ This has practical implications in that therapists differ on whether they should, primarily, treat the patient, the situation or both.

Although the dividing line between brief and long-term psychotherapy is an arbitrary one, empirical considerations have led most writers in this field to consider "brief" any treatment involving usually not more than ten to twenty-five sessions, spread out over a period of three or four months. Other writers allow as many as 40 or more sessions or permit the span of treatment to be six months or longer if the sessions are spaced far apart and their total number is small.^{2,15} Not infrequently treatment is limited, where appropriate, to less than five sessions.^{2,13} Occasionally a pre-established time limit is used.⁸ The empirical considerations referred to above have to do with the observation that as treatment is extended beyond ten to twenty-five sessions, the focus inevitably broadens to include, in addition to the current predicament, examination of the patient's fundamental and long-standing ways of reacting—that is, of his personality or character.

The frequency of the visits usually is once (or twice) a week, although if initially the patient is highly distressed and symptomatic the first several sessions may need to be closer together. The duration of each visit generally is the standard 50-minute hour, and this is likely to be true particularly when the treatment is carried out by a psychiatrist. Recently, however, there has been experimentation with "hours" of lesser duration, and these have been found to be useful and sufficient, especially when the goal of treatment is limited to simple support.^{3,8,14,16}

The Strategies of Brief Psychotherapy

The strategies of brief psychotherapy derive from the often-met need to relieve the patient's suffering and, in particular, his most pressing and disabling symptoms, as promptly and expeditiously as possible. Brief treatment is especially indicated where the patient's distress is not the expression of a long-standing neurotic struggle, but rather of an unfortunate predicament which has noticeably taxed his endurance and social effectiveness and has rekindled an internal conflict, previously dormant or, at least, adequately managed. Premium is placed on brevity and economy of treatment and

this is achieved by deliberate attention to the patient's major current conflict(s) and to the key relationship(s) involved in the patient's current upset. No attempt is made to alter or reconstruct the patient's basic personality or to disturb well-established defensive patterns. The emphasis, always a highly practical one, is on taking care of first things first. The patient is accepted as he is and the aim of treatment is not, primarily, to change him but to alleviate his distress so that he can function more comfortably and effectively in the circumstances in which he finds himself.

When the patient is helped "over a hump," brief psychotherapy regularly becomes crisis therapy. Although the contributions of the past are not totally neglected, the focus primarily is on the present (What ails him now?) rather than on the past (How did he become what he is?) or the future (Where is he going? Is his life fulfilling its basic goals?). These remarks, however, must be qualified. Brief psychotherapy is not limited to removal of troublesome symptoms and alleviation of general distress, nor is more fundamental and lasting "change" the exclusive province of long-term psychotherapy. Depending on the presenting problem, on the vigor and effectiveness of the patient's basic personality, on the favorableness of his social circumstances and on the skill of the therapist, important reorganizations of sectors of the personality can take place and these changes may well go beyond a temporary improvement of the homeostatic balance. In fact, a wide spectrum of results is seen; in some cases major changes in depth take place and the outcome is both enduring and impressive. What is accomplished in brief psychotherapy depends to a large degree on the patient's capacity for working through the issues touched upon during the limited period of treatment. In brief therapy, "working through" is greatly foreshortened for want of time. Actually, much of this process is left to the patient to complete on his own after treatment has stopped, and consequently a later follow-up is particularly important to evaluate the final result.

The Tactics of Brief Psychotherapy

It is proverbial that all is fair in love and war and, one might add also, in brief psychotherapy. In short, a wide variety of techniques²² is available to achieve the goals of treatment and these generally are used freely, depending on the requirements of the particular case (and also the psychotherapist's special predilection). Brief psychother-

apy is an unabashedly expedient affair and from the very beginning everything is used that can help to achieve the desired result quickly. Insight and self-understanding, which play a primary role in most forms of long-term treatment, do not hold a similar position here. Rather, any and all devices are employed that will help the patient to feel and function better and these include:

- Rapidly establishing a warmly positive relationship.

- Ventilation and emotional catharsis.
- Reassurance and suggestion. Occasionally the latter may take the form of hypnosis.

- Exhortation, counseling, advice and environmental manipulation.

- Explanations and educational remarks.

- Drug-giving.

- Desensitization by counter-conditioning techniques, especially for phobias and other focal anxiety responses.

- Interpretative maneuvers. These include clarifications (of feelings, thoughts, attitudes), confrontations and interpretations proper. Occasionally a dream may prove a useful starting point for the analysis of a crucial current conflict.

The devices that will be used in any given instance depend to a large extent on the psychotherapist's personal preference (and level of training). Many achieve very satisfactory results by relying on the two mainstays of brief treatment, namely, the benefits of a positive relationship and adequate catharsis. Others add in varying proportions suggestion, exhortation, explanation, manipulation and drug-giving. Psychotropic drugs can be useful adjuncts to brief psychotherapy: They need to be given in adequate therapeutic dosage and one must keep in mind that while they often alleviate the patient's distress, they do not, by themselves, resolve his problems. Desensitization techniques based on counter-conditioning and other contributions of behavior therapy still have very limited acceptance by the bulk of psychotherapists, although interest in approaches, still quite new, appears to be growing.²⁴ Finally, many psychotherapists employ primarily interpretative maneuvers, which are used similarly as in the more intensive forms of long-term treatment.^{9,13} They emphasize insight and self-understanding and try to go as far in this direction as time and the opportunity for working-through of conflicts allows. Brief psychotherapy, then, need not be grossly manipula-

tive and it is possible to hew fairly closely to an interpretative approach. On the other hand, practically all brief psychotherapists, regardless of persuasion, agree on the need for activity and responsiveness by the therapist: It is his task to help the patient become quickly involved and to define the areas and the issues with which treatment will concern itself.

Indications and Contraindications For Brief Psychotherapy

Brief psychotherapy has much to offer to a variety of patients, yet it is not suitable for all patients or all conditions and there are some for which it is quite unsuitable. The decision as to the appropriateness of brief psychotherapy should be made on *clinical* grounds, that is, on the specific features of the patients' disturbance, although in practice it is often influenced by extraneous factors, the patient's financial resources and the therapist's available time. As Gillman pointed out, "Selection must not be based merely on the absence of some criterion for psychoanalysis, or because a particular therapist needs to feel the power of directive therapy and quick cure, or because the predilection is for limited goals rather than getting to the bottom of things."⁹

Exhaustive discussion of this complex subject is not appropriate here, but it should be emphasized that in speaking about the indications and contraindications for brief psychotherapy we are referring to those conditions and situations where this mode of treatment can be expected to provide reasonably definitive results. On the other hand, the range of indications can be broadened considerably beyond what will be discussed in the following paragraphs, and in practice a wide variety of patients are treated with brief psychotherapy, including many that by more stringent criteria would be regarded as unsuitable.

In those instances where an adequate response is not obtained, provisions are made for long-term treatment or else the patient is seen again for one or more "courses" of brief psychotherapy. The latter approach actually is preferred by therapists who are skeptical about the value of long-term psychotherapeutic efforts and who believe that the main contribution of psychotherapy is to provide support to the patient who is in a "crisis" so that he can endure it without a major regression or breakdown.

Brief psychotherapy probably is best limited to patients of reasonably mature personality and

adequate motivation whose emotional disturbance is focal, acute (rather than chronic), of less than extreme intensity and associated with fairly apparent situational factors. It is highly desirable that the patient, despite his distress (which, in some instances, may be very great) still be able to function in his accustomed social role. In short, this means, primarily, *neurotic* patients, not grossly incapacitated, who see their previous functioning as reasonably satisfactory, or at least not troublesome enough to warrant more extensive investigation. Those who suffer mainly from anxiety, moderate depression or minor hysterical conversions frequently respond remarkably well. Yet, more significant than any one particular symptom or diagnosis is the patient's accessibility and his capacity and readiness for rapid involvement with the therapist.²²

On the other hand, brief psychotherapy is of limited value whenever the person is no longer able to function in his accustomed social role. Here, one specifically wishes to include psychotic patients, those with massive character disorders of long standing (e.g., alcoholics, drug addicts, and the severely unstable and self-destructive), and those with chronic, complex and disabling "psychosomatic" illnesses (e.g., ulcerative colitis, rheumatoid arthritis and the like). Brief treatment of this group, I think, mainly serves to highlight the need for more prolonged treatment. In fact, with these patients brief psychotherapy often serves as an entrée into, and preparation for, more definitive long-term treatment.

Special care must be taken with some depressed patients who are a suicidal risk; brief treatment frequently offers them neither enough protection nor enough time to resolve their difficulty. Schizoid patients who are bland, detached and disenchanted, have trouble becoming involved in brief treatment and often show a very limited response. Patients who are decidedly dependent need the continuing support of an extended relationship. Finally, long-term treatment is called for whenever there is clear and patent indication for personality reconstruction.

Again, not all authors concur in the foregoing, admittedly conservative statement of indications. Burdon, for example, said, "I am convinced that almost all patients can profit from brief psychotherapy . . . [and that] a therapeutic trial . . . [is] indicated in most cases . . .," although later, in stating what he believed to be the optimal indications for brief psychotherapy, he came close to the formula-

tion given above.⁷ In a similar vein, Wolberg said, "The best strategy, in my opinion, is to assume that every patient, irrespective of diagnosis, will respond to short-term treatment unless he proves himself to be refractory to it," but then he, too, allowed himself some of the usual qualifying caveats (e.g., presence of pronounced dependency and immaturity, major character disorders with persistent acting-out, near-psychotic states with massive anxiety).²² He added, however, that he had used short-term methods in treating patients with chronic disease, including obsessive compulsive neurosis and borderline schizophrenia, and had "observed in many gratifying results." In Koebler and Brill's experience, even some quite ill patients (an occasional one with a diagnosis of borderline schizophrenic reaction) responded favorably to what these authors have called Brief Contact Therapy, combined with tranquilizing drugs.¹⁴ Malan expressed belief that patients with disturbances of moderate severity may actually do better than mildly ill patients, especially if they are highly motivated and if they show an ability to work in interpretative therapy.¹⁵ Nonetheless, from his evidence it appears that the poorest therapeutic results were obtained with the sickest patients.

It must be granted also that therapists of special skill and experience are able to broaden the indications for brief psychotherapy and may prove successful in cases which might have failed in more ordinary hands. Storow was able to show that differences in training and experience influence the outcome of psychotherapy (psychiatric residents were more successful than medical students).¹⁹ Yet, this is a difficult assessment, especially when—at the other end of the continuum—one tries to gauge the special attributes of the unusually gifted therapist, clearly a complex and highly individual talent.²⁰ Several authors^{6,15,22} mention the therapist's enthusiasm as especially relevant for the success of brief psychotherapy, and to this we would add also his capacity to engage the patient in a lively, dramatically emphatic way.

Brief Psychotherapy and the General Physician

Brief psychotherapy, potentially, has great significance for the general practice of medicine, but to date probably it has been realized only to a minor degree. Brief psychotherapy offers the non-psychiatric physician an effective instrument to deal with a large segment of his patients' emo-

tional problems. The reason brief psychotherapy can prove so valuable in general medicine is that it is precisely the patients whom the practitioner sees in large number (persons who are distressed, yet functioning) who are best suited for this form of treatment.

The extent to which brief psychotherapy is employed in most medical offices is difficult to assess and depends on how one wishes to define brief psychotherapy. Emotional factors are so intimately involved in all questions of health and disease that, as one general practitioner put it, "The only doctor who can continue his work without using some form of psychotherapy is the one who confines himself to the study of the dead."¹¹ All physicians who treat patients must (and, in varying degrees, do) involve themselves in sympathetic listening and in providing reassurance, advice and drugs. These are time-honored medical functions. On the other hand, the number of general physicians and internists who involve themselves in more formal and specific psychotherapeutic efforts (that is, who offer the patient a planned series of interviews to help him find his way out of a specific quandary) probably is quite small, although no data are available on this point.

During the past 15 or 20 years postgraduate courses on psychiatry for non-psychiatrists have sprung up all over the country. Judging from their popularity, they have been recognized as helpful and needed, yet so far there are only preliminary data^{1,25} by which to assess what influence they have had on patterns of practice or the extent to which graduates of these courses have incorporated psychotherapeutic techniques into their therapeutic armamentarium. The physician is at a disadvantage even if he specifically wishes to learn more about psychotherapy. It is generally underemphasized during medical school. Even these postgraduate courses often do not specifically teach it and restrict themselves rather to patient "management" and other related issues. It is not surprising, therefore, that many physicians, unacquainted with psychotherapeutic techniques, do without them. Yet the climate is changing and there is increasing recognition that the physician needs to have some familiarity with brief psychotherapy. Proof of this is the growing number of journals, including this one, which address themselves to these questions. Only a few years ago it would have been very unlikely that a general medical publication would feature a review article on brief psychotherapy.

Research In Psychotherapy and the Prospects For the Future

We have said already that the current interest in finding psychotherapeutic methods that are both effective and economical has given renewed impetus to research in psychotherapy and that, despite a foundation of knowledge that has already accrued, a number of major questions remain to be more closely defined and, perhaps, answered. There are still many areas where opinion and personal preference take the place of generally shared experience and consensus. The opinions encountered are obviously of varying caliber, some more informed than others; yet, until more systematic data are available, it will be difficult to discard the less valid ones, which still are able to claim professional interest and attention. Of these unanswered questions, the most pressing seem to be the following, although the reader will be able to surmise many more from the material just discussed.

First, the true reach of brief psychotherapy needs to be clarified, with special reference to depth and permanence of results and the extent to which it can be usefully applied to less than optimally suited patients. How often (and to what extent) can true alterations in the structure of the personality be brought about? And how far is this related to the achievement of insight and self-understanding? On this last point there is noticeable disagreement, yet its resolution will have major implications for psychotherapeutic technique. The effect of the psychotherapist's personality and of his level of skill still require close study. The contributions of *brief* group psychotherapy (and, in particular, family therapy) have only recently presented themselves. Are these true alternatives to individual brief psychotherapy? Does each have its *raison d'être* or is it largely a matter of the therapist's predilection, experience or personal comfort?

Finally, one of the most basic questions, whether psychotherapy is truly curative (that is, able to alter and reverse fundamental psychopathology) or primarily palliative (able to console and support) has not been answered to everyone's satisfaction. Each of these questions, as soon as it is approached, breaks down into a number of subsidiary ones which are highly technical and difficult to manipulate experimentally. In fact, the most vital ones are often the most elusive and research efforts not infrequently have been expended on what was measurable rather than what was significant. As Wallerstein remarked, "... the central

dilemma of psychotherapy approach . . . is aptly described in terms of the familiar joke of the drunk searching for his lost keys around the lamppost, not because that was where he had lost them . . . but that was where the light was best. . . ."²¹ Or, as Koegler and Brill point out, "How can understanding be measured? How can change in attitudes be accurately defined when it may take years merely to learn of their existence? What is a reliable measure of disability that can be used for the artist as well as for the bookkeeper . . . ?"¹⁴

Nonetheless, despite these areas of uncertainty and controversy, the current search for dependable answers is a positive and encouraging expression of the vitality of this complex field. Although the data available are necessarily uneven and often lack the hard rigor that some would wish for, psychotherapy has come a long way in almost a century since Anna O. toward establishing itself as the talking cure.

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CASE REPORTS

Auscultatory Sign in Primary Carcinoma of the Liver

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DIAGNOSIS OF primary carcinoma of the liver is difficult to establish before death because signs and symptoms pathognomonic of this malignancy are usually lacking.* The purpose of this article is to characterize a physical sign that apparently is indicative of the presence of a hepatoma. This report describes two cases of hepatocellular carcinoma, each of which was characterized by an abdominal bruit. In both patients, the bruit was heard directly over the enlarged liver, was characteristic of an arteriovenous fistula, and was possibly related, in origin, to the pronounced vascularity of carcinomas of this type.

Reports of Cases

CASE 1.—A 36-year-old man was admitted to the University of California Medical Center for the fifth time 2 November 1965 because of weakness and anemia.

In 1945, he was found on a routine medical examination to be anemic. He remained asymptomatic until 1954, when fatigue developed. He was found to have pancytopenia and a bone marrow aspiration revealed hypoplasia of all marrow elements. Corticosteroid therapy was begun, but numerous blood transfusions (approximately 60

were given from 1954 to 1960) were required to maintain the hematocrit level.

In April 1959, the patient had serum hepatitis, from which he recovered. Splenectomy was performed 2 February 1960. The serum alkaline phosphatase was 10 Shinowara-Jones-Rinehart units (normal, 2 to 6 units).

In February 1965, steroid therapy was discontinued because of the development aseptic necrosis of both femoral heads, and vitamins and fluoxymesterone (Halotestin®) were prescribed. The patient was not icteric, but the liver edge was palpable 2 cm below the right costal margin. A specimen of liver obtained by percutaneous needle biopsy revealed minimal fatty change and hemosiderosis. The alkaline phosphatase was 20 Shinowara-Jones-Rinehart units.

By September 1965 he had become weaker and again required transfusions. Treatment with testosterone enanthate (Delatestryl®), 200 mg intramuscularly weekly, was begun. He was admitted to the Medical Center for the fifth time 2 November 1965 for further evaluation.

On physical examination the patient appeared acutely and chronically ill, although vital signs were within normal limits. His skin was gray, and several spider angiomas and areas of purpura were present. The sclerae were icteric. The lymph nodes were not enlarged, and examination of the heart, lungs and neurological system showed no abnormalities. The liver was palpable 14 cm below the right costal margin and extremely tender. A continuous rough bruit, which was greatly accentuated during late systole, was audible over the central portion of the liver; the sound did not vary with inspiration or changes in the patient's position (Figure 1).

Laboratory tests showed that the platelet count had decreased to 6000 per cu mm. The alkaline phosphatase was 28 Shinowara-Jones-Rinehart units. The serum total bilirubin was 11.2 mg per 100 ml and serum glutamic oxaloacetic transami-

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*Reference Nos. 7, 8, 10, 11, 17, 19, 22, 24, 29.

nase was 268 units. Prothrombin time was 37 per cent and blood ammonia level normal.

Treatment with corticosteroids in large doses (Dexamethasone® 10 mg a day) was begun again. The patient, however, continued to require blood transfusions, the serum bilirubin rose to 17.6 mg per 100 ml, and pancytopenia remained unchanged. On 13 November 1965 he became hypotensive and died.

Postmortem examination revealed hypoplasia of all bone marrow elements, hemosiderosis and a hepatocellular carcinoma. The liver weighed 4600 gm and was diffusely infiltrated by the tumor nodules. Microscopically, the liver parenchyma showed fibrosis, fatty change, chronic inflammatory infiltration and heavy deposition of hemosiderin in both hepatocytes and Kupffer's cells. Death was caused by rupture of a tumor nodule through the liver capsule, followed by massive intraperitoneal hemorrhage. Metastatic lesions were found only in the lungs (microscopically).

CASE 2.—A 60-year-old retired house painter entered San Francisco General Hospital for the

second time 14 April 1965 for chemotherapy. He had been admitted previously (23 January 1965) because of increasing abdominal girth and hematemesis. He had a history of chronic alcoholism, and the clinical findings were characteristic of cirrhosis and portal hypertension. The liver was firm, nodular and enlarged, but not tender. Sulfo-bromophthalein retention was 12 per cent in 45 minutes, the alkaline phosphatase 3.4 Bessey-Lowry units (normal, 0.5 to 3.0 units), and the total serum bilirubin 1.4 mg per 100 ml. Esophageal varices were demonstrated roentgenographically, and a successful spleno-renal shunt was performed 4 March 1965. A biopsy specimen of liver obtained at the time of operation showed the typical changes of portal cirrhosis and a primary hepatoma.

Postoperatively, the patient's condition improved and he was discharged from the hospital. Subsequently, increasing weakness, weight loss, ankle edema and jaundice occurred and he was readmitted to the hospital 14 April 1965.

On physical examination he was observed to be thin and pale and his skin was moderately

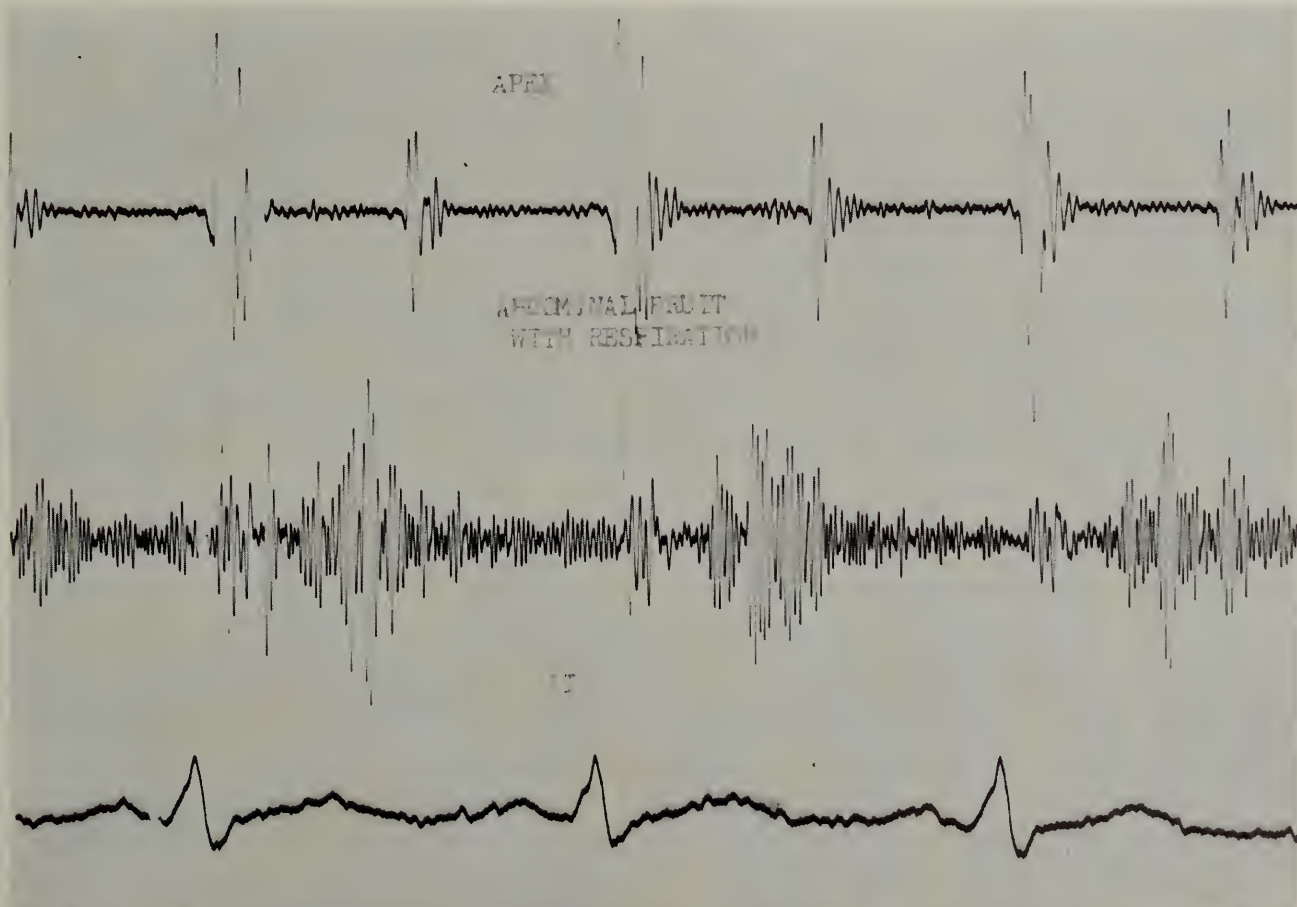


Figure 1.—Apex phonocardiogram in Case 1 (*upper tracing*) with simultaneous recording of continuous bruit over liver (*middle tracing*) and standard lead II of electrocardiogram (*lower tracing*). Note the decided accentuation of the bruit during late systole and the lack of change with respiration.

icteric. The vital signs were within normal limits. The lymph nodes were not enlarged, and no cardiac, pulmonary or neurologic abnormalities were noted. Moderate ascites was present. The liver, which was hard and nodular, was palpable 10 cm below the right costal margin. He had moderate pitting edema of the ankles, slightly greater on the right than on the left. The hematocrit was 27 per cent. Leukocytes numbered 11,800 per cu mm with a normal differential. The platelet count was within normal limits. Alkaline phosphatase was 2.2 Bessey-Lowry units, serum total bilirubin 3.3 mg per 100 ml (conjugated, 2 mg per 100 ml), and the serum glutamic oxaloacetic transaminase 89 units. The prothrombin time was 57 per cent.

The patient was treated with blood transfusions and two five-day courses of 5-fluorouracil, but his condition progressively deteriorated. The alkaline phosphatase increased to 4.3 Bessey-Lowry units and the total serum bilirubin to 9 mg per 100 ml. Hypotension developed and the patient died on 28 May 1965. During the last week of his life a continuous loud harsh murmur, with decided accentuation during systole, was heard directly over the enlarged liver.

Postmortem examination showed portal cirrhosis with moderate fatty change; most of the hepatic tissue, however, had been replaced by a diffuse hepatocellular carcinoma. No evidence of arteriovenous anastomosis or partial arterial occlusion was seen, and the spleno-renal shunt and other vessels were patent. Metastatic lesions were found in the right pleural cavity, in the upper lobe of the left lung, in both adrenal glands and in a thoracic vertebra. The immediate cause of death was rupture of a tumor nodule and subsequent peritoneal hemorrhage.

Discussion

In primary carcinoma of the liver, like most medical and surgical illnesses, definitive treatment depends largely on early and accurate diagnosis. Because of the difficulty in diagnosing this condition, much attention has been given to defining the clinical and laboratory abnormalities that suggest the possible presence of a hepatoma. These manifestations, some of which were present in the two cases described in this report, include rapid deterioration in a patient with preexistent cirrhosis, loss in weight, abdominal pain, progressive enlargement of the liver, increases in the alka-

line phosphatase level and the development of ascites.^{3,16,27} These abnormalities, however, are not singular to this tumor, and at times such protean and even bizarre signs and symptoms as those associated with an "acute abdomen," pulmonary lesions and pleural effusion, fever of unknown origin, collapsed vertebrae or erythrocytosis may indicate the presence of a primary malignancy of the liver.^{2,7,8,14,25,27}

A bruit that develops or is heard over an enlarged liver may also be a manifestation of an occult hepatoma.^{2,4,5,12,21} Continuous murmurs, heard during auscultation of the abdomen, have been discussed extensively as to etiology and significance^{15,28} since 1833 when Pégot described the bruit he heard over the dilated abdominal veins of an alcoholic soldier.²⁰ These murmurs have been noted most frequently in patients with cirrhosis, usually in association with portal hypertension, and in the Cruveiler-Baumgarten syndrome, but they also occur in other conditions.^{1,4} Usually they are continuous soft murmurs, a venous hum or "*bruit de diable*" first described by Laennec in 1819.¹³ Characteristically, they are not heard directly over the liver, nor are they affected by the cardiac cycle. Usually, however, they are accentuated with inspiration, altered by changes in the patient's position and may disappear on use of the Valsalva maneuver or application of pressure with the stethoscope over the auscultated area.^{4,9,26,28} In a few instances, such murmurs have been described as moderately loud and mildly accentuated during systole or diastole.^{4,18,28,30}

In the present cases, the abdominal bruit differed considerably from the more frequently described venous hum. It was heard directly over the liver and was characteristic of an arteriovenous fistula, that is, it had a machinery-like quality; in addition, it was not affected by respiration and was decidedly accentuated during systole (Figure 1).^{6,23} Unlike the venous hum of portal hypertension, which is an extrahepatic murmur, the murmur described in this report is probably intrahepatic and definitely not solely venous in origin.

Although the actual cause of this arteriovenous-like bruit is not known, its character suggests arterial origin. Also, the vascular supply of hepatomas in general is derived entirely from the hepatic artery, thus creating a tissue pattern quite different from that seen in a normal or even a cirrhotic

liver.²¹ This distinctive tissue pattern is found typically in the most frequent form of liver carcinoma, the hepatocellular variety,²⁴ the type present in the two cases described in this report. It is possible that in an enlarging, vascular carcinoma of this type, the arterial blood is frequently shunted into venous channels and occasionally produces a bruit resembling that of an arteriovenous fistula. Alternatively, the bruit might be caused by a partial intrahepatic or extrahepatic arterial obstruction, such as by a tumor nodule. The continuous nature of the murmur heard in the present two cases, however, is evidence against such a mechanism.

Whether this physical sign is a reliable indicator of an underlying hepatoma will require further experience. The findings in the present two cases, however, suggest that the appearance of this type of bruit in a patient with hepatomegaly should alert the physician to the possibility that a primary carcinoma of the liver is present.

Summary

A continuous harsh murmur, characteristic of that produced by an arteriovenous fistula, was audible on abdominal auscultation in two patients with hepatocellular carcinoma. The bruit, unlike the frequently described venous hum, was heard directly over the enlarged liver, was not affected by respiration or changes in position and was greatly accentuated during systole. The present experience suggests that a hepatoma should be suspected in cases in which a continuous arteriovenous-like bruit is heard over an enlarged liver. It is postulated that murmurs of this type may develop as a consequence of the pronounced vascularity characteristic of hepatocellular carcinomas.

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NOTE: Since this manuscript was prepared, another report (Clain, D., Wartnaby, K., and Sherlock, S.: Abdominal arterial murmurs in liver disease, *Lancet*, 2:516, 1966) concerning a similar type of abdominal murmur has been published. It appears that this murmur may be heard over the liver not only in patients with primary hepatomas, but also in those with alcoholic "hepatitis" (an entity which should be easily diagnosed by other means).

Myocardial Contusion in An Eight-year-old Child

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THE MAJORITY OF nonpenetrating crushing injuries of the heart occur in adults, for they are more likely to be involved in traffic and industrial accidents than are children.^{3,6,9} The forces that cause such injuries include: Sudden deceleration of the body against a blunt unyielding object such as a steering wheel, compression by two converging vehicles, impact of a high pressure jet or blast that throws the body against an unyielding surface,³ and the impact of a blunt flying object such as a baseball or a fist. Nonpenetrating chest trauma leading to myocardial injury has been reported more rarely in the pediatric age group.^{7,8}

It is the purpose of this report to present a case of blunt injury to the heart as a result of an accident in a fairly common play situation involving grade school children, and to bring attention to various aspects of diagnosis and management.

Report of a Case

An 8-year-old boy was struck between the 5th and 6th ribs by the tip of a plastic toy "BAT-BAT"* thrown by his 13-year-old brother at close range. The boy screamed, collapsed to the ground and for one or two minutes appeared unconscious. He became ashen and diaphoretic and, after regaining consciousness, began thrashing about with intense anterior chest pain. He was immediately taken to a local medical clinic where his heart rate was found to be 50 per minute and the systolic blood pressure was 70 mm of mercury. He responded promptly to emergency treatment with intramuscular epinephrine and oxygen inhalation.

Submitted 3 February 1967.

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*Manufactured by Reuben Klamer, Beverly Hills, California.

Because of clinical and electrocardiographic evidence of cardiac trauma, he was referred to the UCLA Medical Center for close observation about 28 hours after the injury.

On examination he was observed to be a healthy, alert 8-year-old boy in no distress. There was a small tender erythematous area in the 5th intercostal space 3 cm left of the sternal margin corresponding to the area of impact of the missile. The blood pressure was 90/65 mm of mercury in the right arm, the heart rate 70, respirations 16 per minute and temperature 37.6°C orally. The heart tones were normal except for a short, low grade, apparently innocent, ejection murmur at the pulmonic area. The peripheral pulses were of good quality.

Roentgenographic examination did not reveal any bony or soft tissue abnormalities. The cardiac silhouette was at the upper limit of normal with a cardio-thoracic ratio of 0.53.

The patient remained in the hospital for seven days of strict bed rest. Electrocardiographic monitoring and night-time use of an oxygen tent were carried out on the first two days as precautionary measures. At no time were there signs of cardiac decompensation or angina pectoris, nor was there any abnormality to auscultation. The patient was then released with advice of limited physical activity at home. On visits to the hospital 14 days and 28 days after the incident, the patient remained asymptomatic as he gradually increased his physical activity to a normal level.

Electrocardiographic Findings

Figure 1 shows serial electrocardiograms in chronological order. Shortly after the accident there were sinus bradycardia, right bundle branch block (RBBB) with QRS interval of 0.14 sec, ST segment elevation of the "ischemic type" in V_2 through V_4 with associated deep inversion of T waves, and T waves in V_5 and V_6 were tall and peaked. Lead aVL showed a low voltage RS pattern with a slowly rising ST-T.

Approximately 18 hours after the incident, the heart rate had increased to 80 per minute. The QRS interval had narrowed to 0.06 second and the amplitude of R waves was definitely increased in leads II, III and aVF. There was no evidence of RBBB. ST segment elevation persisted with less inversion of T waves in V_2 through V_4 . There was ST elevation of a junctional type in leads I, V_5 and V_6 . Ectopic ventricular beats presumably of left

ventricular origin were occasionally noted. aVL at this time revealed a QR pattern with Q wave duration of 0.04 second.

Subsequent tracings showed further increase in amplitudes of R waves in Leads II, III, aVF and V₅ and V₆ and corresponding increase in S wave amplitudes in Leads V₁ through V₄. ST-T changes in V₂ and V₄, described previously, tended to improve gradually throughout the hospital stay. Ectopic beats were not seen after the day following injury.

Serum Enzyme Studies

Slight to moderate elevations of serum glutamic oxaloacetic transaminase (SGOT) and lactic dehydrogenase (LDH) levels were noted the day after injury. The former returned to normal by the second day and the latter by the sixth day.

TABLE 1.—Serial Serum Enzyme Levels After Myocardial Contusion in the Case Presented

| Time Lapse After Injury | 28 Hours | 3 Days | 4 Days | 5 Days | 6 Days | 7 Days |
|-----------------------------------------------------|-------------|-----------|-----------|-----------|-----------|-----------|
| Serum glutamic oxaloacetic transaminase | 48 | 24 | | 24 | 18 | 15 |
| Lactic dehydrogenase | 487 | 375 | 365 | 355 | 336 | 325 |

Normal range for SGOT in our institution: 10 to 40 units.
Normal range for LDH: 100 to 350.

The results of enzyme studies are summarized in Table 1.

Comment

Blunt trauma can damage different parts of the heart. Hemopericardium and fibrinous pericarditis can be detected on the basis of clinical evidences of cardiac tamponade or pericardial friction rubs combined with ancillary diagnostic aids. Non-penetrating trauma has been known to produce avulsion of chordae tendinae, of valve leaflets or of papillary muscles, resulting in sudden onset of valvular incompetence.^{8,9} Ventricular septal defects of traumatic origin have been reported in association with both penetrating and non-penetrating injuries.⁴ Ventricular pseudoaneurysm⁵ and rupture of cardiac chambers⁹ following chest trauma have been described.

The present case belongs in a larger group of cardiac trauma—myocardial contusion with or without concomitant ischemic necrosis. Coronary artery damage might be implicated, either by actual severance of the vessel or extensive perivascular hematoma compressing it. Parmley and associates⁹ reported in 1958 that actual intraluminal coronary thrombosis secondary to trauma was very unlikely without antecedent atherosclerosis.

Although electrocardiographic findings in the present case were suggestive of localized anterior

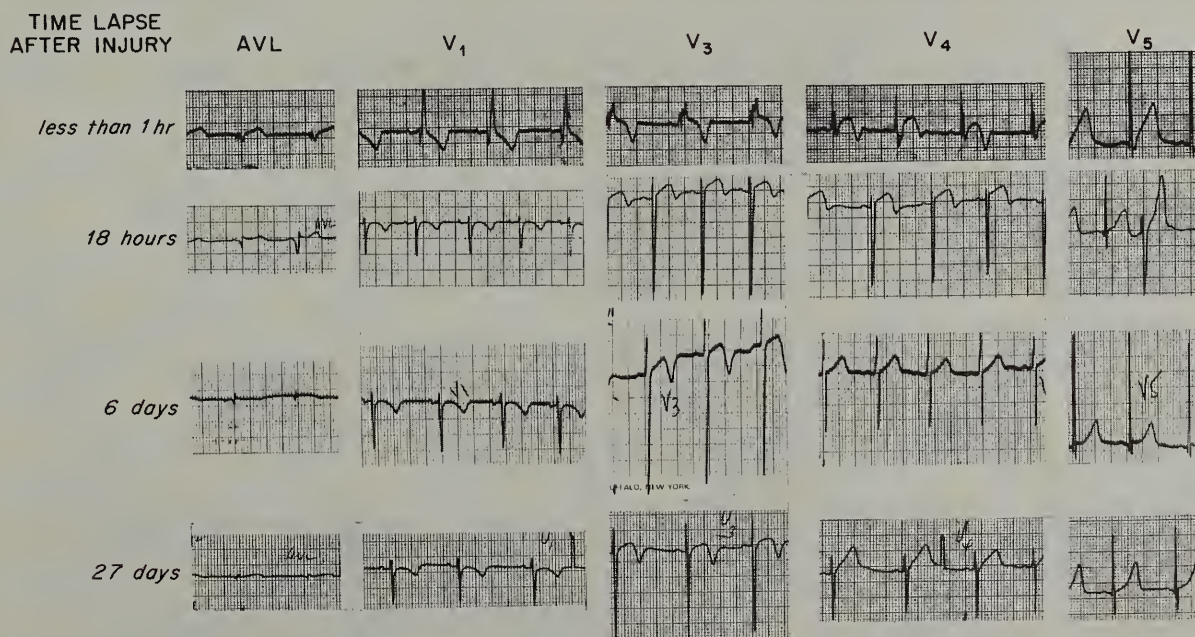


Figure 1.—Serial electrocardiograms following blunt trauma to the anterior chest.

wall ischemic necrosis, it is impossible to differentiate tissue damage due entirely to mechanical trauma from infarction secondary to damage of the left coronary artery branch.

Sinus bradycardia, complete or incomplete bundle branch block and ST segment elevation have been described in myocardial contusion by Barber² and by Goldring and associates.⁷ Transient high amplitude or peaked T waves have also been observed in 10 to 15 per cent of traumatic myocardiopathy according to these investigators. Low voltage QRS complexes (seen in six of eighteen patients) were regarded as strong evidence of myocardial injury.

Though reports of long term follow-up of myocardial contusion are few, most observers agree that prognosis is usually good in mild to moderate cases. Akenside¹ in 1764 described a boy struck by a plate who died unexpectedly six months later, presumably from acute arrhythmia arising from localized full-thickness necrosis of the left ventricle. Bregani³ reported a young man struck and thrown by a high pressure jet who had recurrent angina pectoris and electrocardiographic evidence of myocardial ischemia for three months following the original injury. In another case, residual calcification presumably of a mural thrombus was discovered many years after the original accident.

Finally, one should bear in mind that myocardial contusion is an ever-present menace not only as a result of industrial or traffic accidents, but also in accidents in playgrounds and athletic events. A case of severe myocardial contusion resulting from the act of "spearing" (use of the helmeted head as a battering ram against an opponent) in a football scrimmage has been reported recently.¹⁰

Management

Diagnosis of myocardial contusion may be missed either because symptoms¹⁰ are transient as they were in the present case, or because of the masking effect of more overt symptoms referable to other injured organs.⁹ It is therefore advisable to obtain an electrocardiogram in every case of violent chest trauma. If any abnormality suggestive of myocardial injury is seen, serial tracings must be obtained.

Pathological similarity between myocardial contusion and myocardial infarction secondary to coronary artery disease leads us to regard com-

plete bed rest as a "must" for a period of time sufficient to allow for cessation of necrosis of injured tissue and establishment of healing process. This is ten days to two weeks with mild damage, as in the present case, and up to six to eight weeks in severely injured patients. Severity of associated injuries may also dictate the duration of bed rest. Electrocardiograms, serum enzyme studies including transaminase, lactic dehydrogenase and creatine phosphokinase¹¹ and erythrocyte sedimentation rates obtained at appropriate intervals serve as useful guides. Oxygen therapy may be a useful adjunct in reducing cardiac work in the initial period. Continuous monitoring of the electrocardiogram is important in early detection and treatment of life-threatening arrhythmias. Frequent assessment of pulse, respiration rate and blood pressure would not only alert one to congestive heart failure at its incipient stage but might lead to earlier detection of sudden rupture of ventricular septum or a papillary muscle. These complications may occur hours or days after the initial injury⁸ and are known to cause acute congestive heart failure or pulmonary hypertension or both. Such lesions often require operative repair with extracorporeal circulation.

Anticoagulation is probably not indicated because of the very rare incidence of coronary thrombosis secondary to trauma, especially in young patients. Furthermore, in the presence of concomitant injury to other viscera, use of anticoagulant agents may precipitate or worsen hemorrhage.

Summary

An 8-year-old boy in whom myocardial contusion was caused by a non-penetrating chest injury recovered promptly after an alarming initial shock-like state and serial electrocardiographic changes. Electrocardiographic and blood chemical studies supported the diagnosis of myocardial contusion or ischemic necrosis despite the benign outward appearance of the lesion.

Addendum:

After this report was submitted for publication serum levels of lactic acid dehydrogenase isoenzymes 1 through 5 determined in this patient seven days after the trauma became known to us. Isoenzymes 1 through 3 were well within normal limits, while isoenzyme 4 and 5 were 26 and 37 units (normal range for both: 0 to 15 units). Ele-

vation of LDH isoenzyme 5 is highly specific for myocardial injury.¹²

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demonstration of a cyst "in the area of the seminal vesicle."^{7,8,12,13} Careful review of the literature disclosed only seven cases of clinically discovered and anatomically proved cysts of the seminal vesicle.*

Englisch⁴ believed that seminal vesicular cysts developed from inflammatory closure of small diverticula. He also described various other types of cysts found in this area, such as those arising from Wolffian duct remnants and generally located in the region of the vas deferens at the posterolateral aspect of the bladder, as noted in the report published by Lund and Cummings.¹⁶ Other cysts arising from Mullerian duct remnants are usually midline in position and are attached to the posterior bladder wall; these are further discussed by Coppridge.¹ Cystic dilatation of the utricle may be secondary to stricture of its orifice as was noted in a case reported by Lubash.¹⁵

Voelcker,²² Schwarzwald,¹⁹ and Lloyd and Pranke¹⁴ cautioned against making the diagnosis of seminal vesicular cyst solely from clinical findings and roentgenographic studies. They stressed that anatomic confirmation should be accomplished by surgical operation, demonstrating the cyst to be an integral part of the seminal vesicle. Spermatozoa are usually found in the cystic fluid, but their presence is not diagnostically imperative. Subsequent histopathologic confirmation of seminal vesicular tissue in the wall of the cyst represents final verification.

Report of a Case

A 36-year-old white man, an avowed homosexual, entered Mount Zion Hospital and Medical Center, San Francisco, 24 August 1966 with a six-week history of persistent, painless bloody urethral discharge which made "nickel-sized bright red spots" on his underwear. For several days before admission he had had vague suprapubic discomfort. There were no lower urinary tract symptoms nor gross hematuria nor history of tuberculosis.

The patient had been put in hospital by another physician five weeks previously for evaluation of the same complaints. Microscopic hematuria was present then. Endoscopy had revealed an anterior urethral stricture which was promptly dilated. Retrograde pyelography at that time demonstrated bilateral renal calculi. Our urologic consultation was sought by the patient because the urethral discharge persisted. Past genitourinary history in-

Seminal Vesicular Cyst

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THE PURPOSE of this paper is to report the diagnosis and successful treatment of a seminal vesicular cyst in a patient and to review the literature which establishes this as the eighth such case reported.

Approximately 20 cases of seminal vesicular cysts have been reported. In many of the older reports the lesions apparently were Mullerian duct cysts.^{2,5,6,18,20} More recent reports were based on roentgenographic evidence only, or on surgical

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cluded one untreated episode of transient hematuria four years earlier. There had been multiple episodes of gonococcal urethritis and one episode of syphilis. Apparently all episodes were promptly and adequately treated with penicillin.

On physical examination the only pertinent abnormality noted was indurated seminal vesicles bilaterally. The expressed prostatic secretion contained 4 to 6 leukocytes (and rarely erythrocytes) per high power field. The urine contained 3 to 5 erythrocytes per high power field. A hemogram was within normal limits, as were serum sodium, potassium, chloride, carbon dioxide, calcium, phosphorus, alkaline phosphatase, creatinine, and uric acid. A Venereal Disease Research Laboratory test was negative. Routine bacteriologic cultures of the urine produced no growth. Multiple acid-fast smears and culture studies were also negative for tuberculosis.

An infusion intravenous urogram demonstrated normal renal outlines, with multiple small medullary cysts, many of which contained calcific densities. Retrograde urethrography and voiding cystourethrography demonstrated no abnormality. Endoscopy under general anesthesia revealed a normal bladder and urethra. On retrograde ureteropyelography only a few of the renal medullary cysts filled. Differential phenosulfonphthalein excretion was normal. During bimanual recto-abdominal examination a movable, 4×6 cm cyst was palpated immediately above the indurated base of



Figure 1.—The seminal vesicular cyst is well outlined. Note the retention of radiopaque material within the dilated ampulla of the vas deferens.



Figure 2.—Antegrade right seminal vesiculogram demonstrates the vas deferens and its dilated ampulla, and the initial filling of the seminal vesicular cyst.

the right seminal vesicle. Subsequently, when the patient was awake, the lower end of this cyst was again palpated.

A barium enema revealed a few scattered diverticula of the colon.

An antegrade seminal vesiculogram was performed with the contrast medium injected through a right trans-scrotal vasotomy. Fluid could not be aspirated before the injection. A cyst of the seminal vesicle was demonstrated (Figure 1), as well as dilatation of the ampulla of the vas deferens (Figure 2). There was no efflux of radiopaque material into the prostatic urethra.

On 1 September 1966, under general anesthesia, a suprapubic, extraperitoneal and extravesical exploration was undertaken. The entire cystic seminal vesicle was exposed, as was the dilated ampulla of the vas deferens, the right ureterovesical junction and the base of the prostate. The ampulla was inadvertently opened and clear, light-amber fluid escaped. The entire right seminal vesicle and the attached segment of vas deferens were excised. The postoperative course was uneventful and the patient was discharged from hospital 14 September 1966.

Gross examination of the specimen (Figure 3) revealed that the entire seminal vesicle had become cystic. It measured 3×5 cm. The vas deferens was normal except for dilatation of the ampulla. The cyst wall was 2 to 3 mm thick, with a relatively smooth inner surface (Figure 4). Typical cuboidal cell epithelium of the seminal vesicle was

intact in many areas. There was no significant infiltration of inflammatory cells.

During convalescence, the patient had normal erections and ejaculations. On several office visits spermatozoa were observed in the urinary sediment. Minimal microscopic hematuria has persisted. When last observed, in the fifth postoperative month, the patient had had no recurrence of urethral discharge.

Discussion

Of particular interest in the present case was the presenting complaint of sanguinous urethral discharge, unrelated to micturition or sexual activity and not associated with lower urinary tract obstructive or irritative symptoms. All the previous reports of verified cases of seminal vesicular cyst specified lower urinary tract symptoms as the presenting complaint. The patient reported by Heller and Whitesel also had hematospermia.¹⁰ In the present case the sanguinous urethral discharge probably arose from intracystic pressure, transmitted to the inflamed, strictured ejaculatory duct. It is probable that the hydrops of the seminal vesicle and dilatation of the ampulla of the vas deferens arose from atresia of the ejaculatory duct. The multiple episodes of gonococcal urethritis may have contributed to the ductal atresia. In a case he reported, Zinner²³ noted atresia of the ejaculatory duct resulting from extensive scar formation.

It is to be emphasized that cysts of the seminal vesicle are quite uncommon. Hyams, Kramer and McCarthy made postmortem studies of many hundreds of seminal vesicles in cadavers with gross evidence of inflammation in this region.¹¹

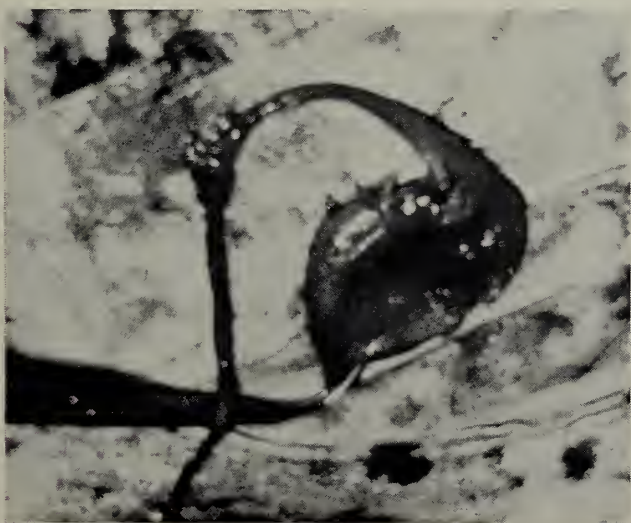


Figure 3.—Gross surgical specimen. The clamp is on the severed ejaculatory duct.



Figure 4.—The cystic seminal vesicle has been bivalved. Note the relatively smooth inner surface.

Cysts of the seminal vesicle were not found. They emphasized that the ejaculatory ducts were always involved in posterior urethral inflammation. McMahon studied 100 seminal vesicles and reported no cysts.¹⁷ Nevertheless, we subscribe to the general thesis that the more diligent a search for a given pathological entity, the more frequently the condition will be encountered, including cysts of the seminal vesicle.

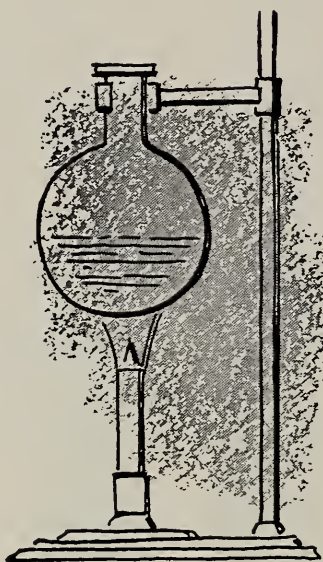
As a final and passing comment, it is noted that the authors of this report, two urologists and an internist were in agreement that the presence of medullary sponge kidneys in this patient was coincidental rather than a manifestation of a more generalized cystic syndrome.

Summary

A case of anatomically proved seminal vesicular cyst is reported, the eighth in the literature. The presenting symptom was bloody urethral discharge unrelated to micturition or sexual activity. A brief review of the literature was made, emphasizing anatomic confirmation as the diagnostic necessity.

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Ulcerative Colitis with Liver Disease

These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California Medical Center, San Francisco. Taken from transcriptions, they are prepared by Drs. Martin J. Cline and Hibbard E. Williams, Assistant Professors of Medicine, under the direction of Dr. Lloyd H. Smith, Jr., Professor of Medicine and Chairman of the Department of Medicine.

DR. AARONSON*: The patient, a 24-year-old male graduate student, had a history of abdominal pain, bloody diarrhea and weight loss beginning ten years before the present admission to hospital. Eight years before admission a diagnosis of ulcerative colitis was made after barium enema and sigmoidoscopic examination. The symptoms abated until four years ago when the patient was put in hospital for recurrence of diarrhea and weight loss of 30 pounds. Three months before the present admission, he was found to be anemic. Physical examination revealed enlargement of the liver. On sigmoidoscopy the colon was noted to be edematous, friable and ulcerated. Serum bilirubin and alkaline phosphatase levels were elevated. One month before the present admission he was put in hospital because of injury in a fall from a bicycle. On examination there, fever, splenomegaly and elevation of serum alkaline phosphatase were noted. He denied arthritis, dermatitis, iritis, jaundice or exposure to toxic chemicals. He also denied any drug administration or exposure to patients with infectious diseases. It was then that he was transferred to this hospital for further studies.

The blood pressure was 135/65 mm of mercury, the pulse 88 and regular and temperature 38°C (100.4°F). The skin was not icteric and no lymph nodes were palpated. The liver, felt 1 cm below the right costal margin, was firm and non-tender. The spleen was tender and was felt 3 cm below the left costal margin. The remainder of the abdominal examination was within normal limits.

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Hemoglobin was 10.1 gm per 100 ml, packed cell volume 35 per cent, sedimentation rate 28 mm in one hour, leukocyte count within normal limits, with 8 per cent eosinophiles. Serum cholesterol was 202 mg and serum bilirubin was 1.6 mg per 100 ml (direct 0.6 mg), alkaline phosphatase 22 Shino-wara-Jones-Reinhardt units, bromsulphthalein retention 25 per cent, serum albumin 2.7 gm and serum globulin 3.4 gm per 100 ml, and serum 5-nucleotidase 21 units (normal less than 1.5 units). The prothrombin time varied between 40 and 60 per cent.

Sigmoidoscopic examination revealed friable, bleeding rectal mucosa and no masses. Bone marrow examination showed absence of iron stores. A needle biopsy of the liver was interpreted as within normal limits.

The patient was treated with prednisone by mouth, 15 mg per day, hydrocortisone, 100 mg in oil by enema every evening, and sulfasoxazole 2 gm three times a day. He was discharged with a diagnosis of ulcerative colitis and probable pericholangitis.

DR. RUSSELL*¹: There are several interesting x-ray findings in this patient. The initial chest film showed streaky densities in both apices. What appears to be a small effusion on the left, which showed up well in the oblique projection, might also have been pleural thickening. Barium enema demonstrated a large spleen displacing the splenic flexure medially and anteriorly. The barium enema

*¹Warren Russell, M.D., Assistant Professor of Radiology.

studies were otherwise unremarkable. There was no evidence of ulceration of the colon at this time, and the mucosal pattern appeared normal. A persistently narrowed area, although changing somewhat in shape, was demonstrated in the region of the recto-sigmoid junction by multiple spot films. Oral cholecystograms on two successive days showed poor visualization of the normal gallbladder. No gallstones were seen.

Hepatic Disease as a Complication

DR. SMITH*²: Actually there are many aspects of ulcerative colitis which could be presented, but we decided this morning to give major emphasis to one of the complications of ulcerative colitis—namely, hepatic disease. We have asked Dr. Howard Shapiro to open this discussion. We would particularly be interested in knowing how frequently this complication occurs and how important it is in the prognosis of the disease.

DR. SHAPIRO*³: That is a large order. I think that in our present state of knowledge, the description will be primarily phenomenological.

Briefly, this 24-year-old man had a ten-year history of very mild ulcerative colitis. He had one severe exacerbation before there was any suspicion of liver disease. The liver disease was really discovered by serendipity. The patient was asymptomatic but the physician was rather bothered by a low hemoglobin, and investigation of that problem ensued. When the patient was first studied, he had conjugated hyperbilirubinemia and an elevated alkaline phosphatase. Again he remained asymptomatic until the accident which precipitated his hospital admission. We were able to confirm the elevation of alkaline phosphatase. We were fairly certain that this was due to liver disease because there was pronounced elevation in the serum 5-nucleotidase, a test which is more specific for obstructive liver disease since it is not affected by bone disease. He also had bromsulphthalein retention of 25 per cent, which probably accounts for the poor visualization of the gallbladder. Results of the other tests of hepatic function were quite normal. Of interest to me was the fact that the blood cholesterol was normal. There will be further comment on this finding later. Initially he had a febrile course and later became afebrile on no specific therapy. He was treated vigorously

with rectal instillations of steroids, oral sulfonamides and systemic steroids, and was then discharged. The dramatic thing about this patient is not the clinical course, rather it is the abnormalities noted on chemical studies of the liver that pique our curiosity. I am sure that the patient would be just as well off and just as happy if he had never entered the hospital nor had the investigations carried out.

We have known for a number of years that liver disease has been associated with ulcerative colitis. The initial studies on the relationship between liver disease and ulcerative colitis were done mostly on necropsy material supplemented with infrequent data on surgical biopsy of the liver. These early studies,⁶ in the late 1940's and early 1950's, on the association of liver disease and ulcerative colitis were necessarily biased by the manner in which these specimens of liver were obtained for examination. In patients with ulcerative colitis and liver disease, a 50 per cent incidence of fatty liver was found in the autopsy series. The fattiness of the liver was considered secondary to malnutrition, protein loss through the rectum and a generalized toxic state. Generally the degree of fattiness found at autopsy in ulcerative colitis parallels the severity of the disease. It is a nonspecific finding. In these early studies the incidence of cirrhosis was 7 per cent, primarily postnecrotic rather than Laennec's type. Considering the incidence of fatty liver, Laennec's cirrhosis is quite rare in ulcerative colitis. Biliary cirrhosis was noted infrequently. These early studies shed little light on the pathogenesis of liver disease in ulcerative colitis.

In 1952, the first communication on needle biopsy of the liver in a series of patients with ulcerative colitis appeared from the Mayo Clinic.² Kleckner and coworkers, the authors of the report, were the first to consider pericholangitis as a distinct entity in ulcerative colitis. In 32 cases of liver disease and ulcerative colitis, biopsy demonstrated fatty liver in 13, cirrhosis in six and pericholangitis in six. These investigators felt that the cause of the pericholangitis in these patients was secondary to bacteria and toxic products reaching the liver through the portal vein. In 1959 similar observations were reported in Australia by Rankin and coworkers⁷ who for the first time characterized pericholangitis as a lesion in ulcerative colitis. They too considered it secondary to portal bacteremia. In 1959 Rankin and his coworkers treated six patients with broad spectrum antibiotics. Initially they noted promising results in that these

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*³Howard Shapiro, M.D., Assistant Clinical Professor of Medicine.

patients did have some improvement of liver function and less frequent bouts of fever, jaundice and pruritus. Later they themselves came to doubt that the tetracyclines really have much to offer in the treatment of pericholangitis associated with ulcerative colitis.

More definitive observations were made by Mistilis^{3,4} and his associates in Australia who published two excellent papers in 1965 on the clinical aspects, pathogenesis, pathology and some etiologic consideration of pericholangitis. Their work had been carried out carefully over a 15-year period. Among 450 patients with ulcerative colitis (this was their clinic population) 28 also had pericholangitis. The patient presented today fits well the clinical description of those patients. Thirteen of the 28 patients were completely asymptomatic. The disease came to light because of enlargement of the liver, and all had elevated alkaline phosphatase determinations. None of the asymptomatic patients had any other stigmata of liver disease.

The next largest group of patients had episodic, cholestatic jaundice. These patients had episodic attacks of jaundice and pruritus associated with elevation of the alkaline phosphatase level. These episodes would vary from weeks to months but they were never very dramatic. There were no pre-icteric symptoms, and there were long asymptomatic periods between these episodes of jaundice and pruritus.

The third group of patients had cholangiolytic attacks. They had bouts of pruritus, fever, abdominal pain and mild toxemia associated with some liver tenderness. Icterus was variable. Again, the alkaline phosphatase level was always elevated. These attacks were rather sudden in onset without pre-icteric symptoms, and lasted for days to weeks. There were long asymptomatic periods between these attacks, some as long as four to twelve years.

There were many patients who had cholangitic attacks with long asymptomatic periods and then a cholestatic episode as well. The clinical differentiation among these three groups is really a stationary one; at any one time, one can differentiate among these three groups, but longitudinally any one patient may have all three types of pericholangitis in association with ulcerative colitis. The ulcerative colitis in all of the patients that Mistilis described was very mild. Such is the case in the young man presented today. In patients that did have severe episodes of ulcerative colitis, these

episodes usually antedated the diagnosis of liver disease. The colitis was usually left-sided; universal involvement was unusual. Mistilis and his coworkers noted in their cases something that was not observed in today's patient—that the extracolonic manifestations of ulcerative colitis were quite frequent. A number of their patients had transient arthralgia. Three had chronic active hepatitis in association with a positive lupus erythematosus phenomenon.

In all of their patients the alkaline phosphatase level was elevated. Hypercholesterolemia was usual but by no means universal, and an increase in bromsulphthalein retention was common. The transaminase determinations, if they were elevated at all, were very slightly elevated to a level less than 200 units. The serum electrophoretic pattern was frequently normal but occasionally hypergammaglobulinemia was present. The flocculation tests were all normal.

Three Categories of Pericholangitis

In their description of the pathologic features of pericholangitis, Mistilis and his coworkers divided the cases into three categories: Acute, subacute and chronic. The acute phase is characterized by cellular infiltration in the portal tracts, some swelling and edema of the finer biliary structures, and generally some dilatation and prominence of the lymphatic structures within the portal tracts. In the subacute phase there is a pronounced decrease in the cellular infiltration and edema of the portal tracts, and a general increase in the connective tissue and in fibroblastic proliferation in the portal tracts. There is often some hyaline change in the ductal walls.

As this progresses into the chronic phase, there is a pronounced decrease in the inflammatory cell response in the periportal areas. Indeed, what seems to happen is a shift of the zone of inflammatory cell response out of the portal triads and into the junctional zone between the portal tracts and the adjoining parenchymal cells. In the chronic phase, it can resemble chronic active hepatitis because there is actual hepatic cell necrosis and inflammation in the periportal areas. In this chronic phase there is a decided increase of periportal and circumductal fibrosis, leading to a stellate appearance of the portal triads. Lymphangectasia is present. Because of the shift of the junctional inflammatory zone to the liver parenchyma, there is piecemeal necrosis of hepatic parenchyma which suggests frank cirrhosis. The

chronic phase of the pericholangitis can resemble postnecrotic cirrhosis or chronic active hepatitis, and indeed six of their twenty-eight patients had postnecrotic cirrhosis and eight had chronic active hepatitis. The chronic active hepatitis was almost always associated with hypergammaglobulinemia, and in three cases the result of a test for lupus erythematosus was positive.

It is interesting that the Mistilis group repeatedly performed liver biopsy on their patients over a period of 15 years and found no false sampling. In cases of metastatic carcinoma our own experience in liver biopsy suggests a positive diagnosis in 60 to 70 per cent. Similar findings occur in sarcoidosis as well. Frequently in cirrhosis the specimen is from a perfectly normal area and the cirrhotic area missed. That they found liver biopsy diagnostic in all cases is quite remarkable.

Mistilis expressed belief that the progression of acute to subacute to chronic pericholangitis is inevitable.⁵ In all cases, there was slow but definite progression of disease. Four patients had colectomy, five were given antibiotic therapy over long periods and several were treated with a low dose of corticosteroids. Despite these various modes of therapy the liver disease progressed.

The Possible Role of Bacterial Infection

There were several factors that I have mentioned in the description of this disease that pique one's curiosity about its genesis. I don't think that anyone who has dealt with this disease feels that he can make definite statements about the cause, but the findings of perilymphangitis and periphlebitis and intense portal inflammatory responses do lend support to the possibility that bacterial infection has a role in triggering the illness. The portal blood is usually sterile but portal bacteremia has been demonstrated in many patients with ulcerative colitis. The onset of this pericholangitis might be associated with an acute infectious process. However the fact that it does not respond to antibiotic therapy or to total colectomy suggests that once the disease is established in the portal tract it is self-perpetuating.

These conjectures about a self-perpetuating liver disease triggered by an acute infection are reminiscent of chronic active hepatitis, or so-called lupoid hepatitis, which is considered by most observers to be an autoimmune disease. In chronic active hepatitis it has been suggested that the virus particle damages the live cell, which somehow

induces it to act as an antigen against itself, leading to a self-perpetuating mechanism that is triggered perhaps by acute viral infection. In the pericholangitis of ulcerative colitis, I suppose one could also consider an autoimmune phenomenon to explain the progressive nature of this disease. If this is the case, one might expect to see hypergammaglobulinemia more commonly. One would also expect a better response to corticosteroid therapy.

Varying Rate of Progression

DR. SMITH: Thank you very much, Dr. Shapiro. The most surprising thing to me in your discussion was the prognosis. I was not aware that a patient such as we have seen today with relatively minor alterations of liver function would almost invariably have progressive attacks leading to severe hepatic derangement. What would you expect the time course to be?

DR. SHAPIRO: I have mentioned that the course is invariably progressive, but that the time that it takes for the progression to occur is quite variable. Some patients in Mistilis' series have gone 15 years between attacks of cholangitis, some have had a much more rapid progression. Since the liver biopsy in today's patient has been interpreted as normal and since he is relatively asymptomatic now, he may show his first signs of progression 15, 20 or 25 years from now. In that sense, life itself is a progressive disease.

DR. SMITH: Dr. Carbone, has this been your experience in ulcerative colitis?

DR. CARBONE*4: Yes. We have several patients who have had relative stability of ulcerative colitis for 15 years. During this period of time, three patients of this group have developed cirrhosis and progressive liver failure. The terminal stage of their liver disease is portal cirrhosis. However, at varying times one will find pericholangitis and a significant incidence of sclerosing cholangitis.

Treatment of patients with ulcerative colitis and liver disease has been disappointing with respect to the progressive changes in the liver. Even though these patients have been treated continuously with steroids, either systemically or by retention enemas and continuous sulfonamides, the natural history of the liver disease has been progressive. This is in spite of excellent control of colitis and, in many instances, a complete reversal

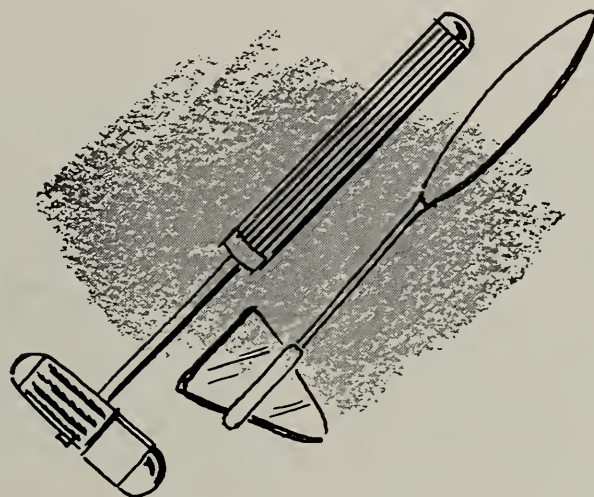
*⁴John V. Carbone, M.D., Professor of Medicine.

of the inflammatory lesion of the colon.

There is reason to believe that the combination of ulcerative colitis and liver disease may be a different disease than idiopathic ulcerative colitis. These patients, as a group, tend to have a milder form of colitis and more extracolonic manifestations of the disease. They lack the usual response to colectomy and oftentimes the colitis becomes apparent after the liver disease has been documented.

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California Medicine

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EDITORIAL

CMA's Position on Medi-Cal's Straits

IN TAKING the position it has adopted with regard to the proposed restriction of services under the Medi-Cal program, the California Medical Association was guided by a wish to make the program work as well as possible during a trying—and, it is hoped, temporary—budgetary shortage. Fully as important is the consideration that from this position CMA can best use its influence to steer Medi-Cal back to being the mainstream medical care plan for medically needy Californians that it was intended to be when legislation creating it was enacted.

The association endorsed that legislation in the belief that it offered a means of providing medical care through the regular channels of medical practice to persons who otherwise could not be served in that manner. It still endorses the legislation and the purpose.

When the state administration in Sacramento changed at the beginning of this year, CMA offered its counsel and cooperation to Mr. Spencer Williams, the new administrator of California's Health and Welfare Agency, particularly with regard to Medi-Cal, which was just beginning to operate and was feeling some of the pains of newness. Soon after mid-year, Mr. Williams reported that the revenues available were inadequate to provide all the services encompassed in the Medi-Cal program, and as a solution he proposed emer-

gency regulations limiting the kinds and the extent of health services to fit the available funds. He discussed the proposal with CMA officers and the Council. The Council accepted his fiscal appraisal and pledged the association's cooperation to help deliver the highest possible quality of medical care under regulatory limitations which the Council looked upon as "an interim measure under the current fiscal restrictions imposed by state and federal law."

We well recognize that this position is not dynamic or dramatic. But it need not be, for we believe that the Medi-Cal plan is medically and sociologically sound and that, whatever the reason for the present fiscal difficulty, the courts, the administration and the legislature will, among them, supply the action necessary to bring about a solution that will give the program the support it warrants.

A successful challenge in the courts of the legality of the regulations will not remove or remedy the fiscal problems confronting the program. Other approaches to the matter will undoubtedly be proposed and studied in the coming weeks.

Meanwhile the California Medical Association stands ready to consult with representatives of all branches of government and to use the channels of communication with its members where its help can be useful in promoting good medical care for the people of this state.



California Medical Association

NOTICES AND REPORTS

Council Meeting Minutes

534th Meeting

Tentative Draft: 534th Meeting of the Council, Los Angeles, Airport-Marina Hotel, 8 July 1967.

The meeting was called to order by Chairman Miller at the Airport-Marina Hotel on Saturday, 8 July 1967, at 9:45 a.m.

A quorum was present and acting (full roll call, including names of invited guests, appears in Item 37).

1. Minutes for Approval

The minutes of the 533rd meeting of the Council, held 27 May 1967, were approved as distributed.

JOHN G. MORRISON, M.D. President
MALCOLM C. TODD, M.D. President-Elect
WILLIAM F. QUINN, M.D. Speaker
JOSEPH F. BOYLE, M.D. Vice-Speaker
ALBERT G. MILLER, M.D. Chairman of the Council
HAROLD KAY, M.D. Vice-Chairman of the Council
HELEN B. WEYRAUCH, M.D. Secretary
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2. Appointment of New Executive Director

ACTION: Voted to approve Howard Hassard's request that he resign as Executive Director (continuing as Legal Counsel).

ACTION: Voted to appoint Robert L. Thomas (previously Associate Executive Director) as Executive Director of the California Medical Association.

3. Payment to Physicians in County and Teaching Hospitals Under Medi-Cal

President Morrison reported that on 19 July the Health Review and Program Council would be considering recommendations relating to Section 32.6 of the 1967 State Budget Act (affecting payment to physicians rendering services under Medi-Cal in county and teaching hospitals). The Council reviewed CMA's previously adopted position that Title 18 regulations governing reimbursement of physicians rendering identifiable services in a county or teaching hospital setting (submission of attending physicians' bills on a reasonable charge basis with the amount of the charge to be determined by the carrier in the same manner and under the same rules as for all other physicians) also should be utilized in California's implementation of Title 19 (Medi-Cal).

ACTION: Voted to reaffirm CMA's position regarding payment for physician services in county and teaching hospitals under Medi-Cal and to express this reaffirmation to the Health Review and Program Council.

4. Contractual Relationships with Consumer Groups

Following discussion of possible problems that could arise if segments of medicine within Cali-

fornia enter into direct economic relationships with consumer groups without the consultation and advice of the prepayment organization officially sponsored by CMA (California Blue Shield), the Council adopted the following position:

ACTION: *Voted to urge component societies, medical specialty organizations, or other segments of organized medicine in the state to consult with California Blue Shield before entering into direct economic relationships with consumer groups.*

5. Acceptance of Federal Grants

After considering the need for establishing CMA policy regarding acceptance of Federal grants, the Council:

ACTION: *Voted to approve CMA's considering acceptance of Federal grants on a project-by-project basis.*

ACTION: *Voted to request the board of the California Medical Education and Research Foundation (CMERF) to prepare broad criteria to be used as guidelines in determining when federal funds should be considered, sought and recommended to be accepted (to be brought to the Council for approval).*

6. Request from Northern California Kidney Foundation

Chairman Miller reported that CMA had received from the Northern California Kidney Foundation a written request to use CMA's addressing facilities in their mailing of programs and pre-registration forms for the second annual Symposium on Kidney Disease 17 October 1967, Whitcomb Hotel, San Francisco. Doctor Miller pointed out that it was CMA policy to grant approval to such requests when they come from medical organizations sponsoring educational programs.

ACTION: *Voted to approve the request from the Northern California Kidney Foundation.*

7. Newly Elected American Medical Association Leaders

Chairman Miller expressed the pride of the CMA in having two newly elected AMA leaders from California: Dwight L. Wilbur, M.D., AMA President-Elect, and Burt L. Davis, M.D., member AMA Board of Trustees. It was pointed out that a meeting of the AMA Board precluded either physician from attending this meeting of the Council. However, Chairman Miller read a letter from Doctor Davis in which he expressed his appreciation for the support of the CMA Delegation to the AMA and the Council for his election. Doctor Davis' letter also pointed out that

Doctor Wilbur's election was uncontested and expressed confidence that he would do his usual excellent job in his new position of representing medicine for the entire nation.

8. Report of the President

President Morrison reported on the success of the CMA-Blue Shield Congressional Visitation, made 15 and 16 June in Washington, D.C. He stated that new avenues of communications had been opened in Washington—with friends of medicine as well as those who, in the past, have not seemed to understand medicine's position in health legislation. Doctor Morrison stated that the contacts made with staffs of Congressmen were as valuable, if not more so, than those made with the Congressmen themselves. Doctor Morrison said that this type of project should be followed in the future by similar efforts. Mr. John Pompelli in particular and the AMA Field Service in general were commended for their excellent help. Mr. Will Babb of the California Blue Shield staff also received special commendation for his work on the project. President Morrison's comments were echoed and enlarged upon by Doctors Miller, Boyle and Wilbur.

President Morrison also reported that plans for the meetings with component society presidents (approved by the Council 27 May 1967) were well underway, with a meeting of northern county presidents scheduled for 26 and 27 August and a meeting of southern county presidents scheduled for 30 September and 1 October. He said that an informal meeting of all component society presidents would again be held in conjunction with Annual Session next year. A date for the next Annual Conference of Component Society Officers was discussed, with the following result:

ACTION: *Voted to hold the next annual Conference of Component Society Officers in November 1968.*

9. California Medical Education and Research Foundation

Doctor Morrison discussed the allocation of monies recently received by the California Medical Education and Research Foundation (CMERF). With Council concurring, the \$75,000 gift from Audio-Digest Foundation will be used according to the following decisions by the CMERF Board, which voted to authorize distribution of \$2,500 to the LACMA library for a scholarship for a medical librarian trainee, \$30,000 to medical

schools to support departments of continuing education (specific policy for allocating this money to be determined by the Scientific Board), and \$40,000 for undergraduate merit and achievement scholarships for students entering the health fields. The new program will be called "The California Physicians Scholarship Fund." (The remaining \$2,500 is to be allocated later.)

Doctor Morrison also announced that CMERF had accepted a contract proposal from the Public Health Service to sponsor a conference in November on behalf of 13 western state medical associations that will explore "Future Directions and Decisions in Medical Care."

10. *Report of the President-Elect*

President-Elect Todd commented on his recent visits to physicians in northern counties and other meetings, including a national AMPAC Workshop. As chairman of the Committee on Committees, Doctor Todd gave a brief informational report. He mentioned several positions which are now open and announced that Doctor John Connolly, who was a consultant to the Committee on Cardiovascular Disease, now becomes a member of the committee by virtue of his membership in CMA.

11. *National Conference on Medical Care Costs*

Thomas C. Paton, president of California Blue Shield, presented a brief report on the National Conference on Medical Care Costs recently held in Washington, D.C. He stated that the conference did not attempt to reach any conclusions, rather, it served to alert those in the health care industry that drastic changes are going to evolve more rapidly than many would have supposed. There was grave concern expressed over the fact that in the last 10 years the consumer price index has risen just 19 per cent, while medical care costs have risen 42 per cent. Mr. Paton pointed out that throughout the conference, the terms "medical care costs" were erroneously used when "health care costs" would have been appropriate terminology. Mr. Paton said that he felt it would be a good idea to express to the national administration that Medicine seeks broader involvement in conferences of this type.

12. *Reports from Medical Schools*

Doctor Thomas Gonda, associate dean of Stanford University School of Medicine, expressed

appreciation for the allocation of CMERF monies for postgraduate and undergraduate physician education. He also announced that the Commonwealth Fund had made a \$500,000 grant to Stanford so that it could conduct a study of health care within the teaching hospital setting. Doctor Gonda expressed hope that results of the study would contribute innovations in health care.

Doctor Franz Bauer of USC School of Medicine made a progress report on USC's grant under P. L. 89-239. He announced that Doctor Donald Petit had been appointed as director of the resulting regional medical program.

Doctor Warren Bostick of UC-California College of Medicine and Doctor John Dillon of UCLA also made progress reports concerning their respective medical schools.

All of the medical school representatives expressed concern over section 32.6 of the 1967 State Budget Act (affecting payment to physicians rendering services under Medi-Cal in county and teaching hospitals). President Morrison assured them that their concern was shared by CMA (see item 3 of these minutes).

13. *UCLA School of Public Health*

Doctor L. S. Goerke, dean of the UCLA School of Public Health, commented on progress at his school, stating that the objective was to move from an undergraduate emphasis to an emphasis on master's and doctoral candidates. He stated that he felt the UCLA School of Public Health had the potential of being the strongest one in the country because of its close relationship with medicine.

14. *State Health and Welfare Agency*

Mr. Spencer Williams, administrator of the Health and Welfare Agency, reported to the Council on the current fiscal status of the Medi-Cal program and expressed concern that further program adjustments may become necessary. He said that these could fall in three different areas: (1) modification of eligibility requirements, (2) changes in the scope, amount or duration of services, and (3) limitation in the prices paid for services. He said that the agency was investigating the possibility of instituting a system of partial payment by patients for certain services, but that present Federal regulations precluded this.

Mr. Williams also commented briefly on A. B. 1567 (relating to California implementation of

Public Law 89-749—Comprehensive Health Planning). He expressed concern that the bill could grant inappropriate duties to the State Health Planning Council.

On the subject of mental health, Mr. Williams reported that the governor had recently met with representatives of concerned voluntary organizations. Mr. Williams pointed out that the budgeted amount for mental health in 1967-68 (\$203 million) is only \$3 million less than the amount budgeted for 1966-67. He also stressed that emphasis has shifted to the Short-Doyle concept of providing services to the patient in his own community. Mr. Williams presented the Council with charts showing that since 1960, the patient population in state mental institutions has decreased from 36,000 to 21,700, while the staff has increased in the same period of time. He said that under projected continuing decrease in the patient population, the current ratio of one staff person to every 2.69 patients will be maintained.

15. *State Department of Public Health*

Doctor Lester Breslow, director of the Department of Public Health, gave a progress report on certification of facilities under Medicare, stating that 535 out of California's 565 licensed general hospitals have now qualified. Almost two-thirds of the licensed nursing homes in the state have now qualified, he said, even though only one-third were expected to meet Medicare standards. Over 100 home health agencies and 553 laboratories have been given certification.

Doctor Breslow also described the department's efforts to prepare for the new proficiency testing requirement for independent laboratories under Medicare.

Doctor Carl Anderson pointed out that 269 independent laboratories now have a proficiency testing requirement for certification because they are engaged in interstate commerce and do not have medical directors who meet certain criteria. Doctor Anderson expressed the hope that proficiency testing for other laboratories would be approached on a voluntary basis at this time.

16. *Social Security Administration*

Mrs. Mercia Kahn, regional director of the Bureau of Health Insurance, Social Security Administration, reported that 18 per cent of the nation's extended care facility beds certified for Medicare are in California—with a ratio of 28.6

beds for every thousand Medicare participants. The national average, she said, is 14 beds for every thousand. Mrs. Kahn reminded the Council that Medicare had its first anniversary on 1 July 1967, and offered to supply a summary of the first year's statistics to any person who wished this information. She stated that although the statistics are quite impressive, the Social Security Administration realizes that many problems still need to be worked out under the program. Concluding her remarks, Mrs. Kahn thanked the CMA for its help during Medicare's first and difficult year.

On behalf of the CMA, President-Elect Todd expressed appreciation to Mrs. Kahn for her fine cooperation with the physicians of California.

17. *Woman's Auxiliary to the CMA*

Mrs. Dorothy Flood, president of the CMA Woman's Auxiliary, briefly reported on the recent AMA convention in Atlantic City, stating that WACMA had again won top honors for AMA-ERF contributions. In addition, she said, the Los Angeles County Woman's Auxiliary won a special award for the largest contribution from an auxiliary of over 500 members. Mrs. Flood thanked the CMA Delegation to the AMA for hospitality extended to auxiliary members during the national meeting.

18. *California Nurses' Association*

Mrs. Helen Hancock, president of the California Nurses' Association, discussed recent activities of her association in the areas of health manpower and comprehensive health planning. She also reported that the CNA had been granted exclusive rights to represent nurses in Veterans Administration facilities.

19. *California Medical Assistants Association*

Miss Helen Goldman, president of the CMAA, thanked CMA for appointment of outstanding physicians to the CMA Liaison Committee to the CMAA. She also drew attention to the national conference of the American Association of Medical Assistants, which CMAA will be hosting on 11 to 15 October 1967 in Los Angeles at the International Hotel. She stated that this should give an excellent opportunity for promotion of membership in California and asked for CMA guidance and support. Chairman Miller assured Miss Goldman that CMA fully supported the membership efforts of the CMAA and stated that one sug-

gested way in which CMA could help in current efforts would be to publicize the national convention in *CMA News*.

20. *California Committee on Regional Medical Programs*

Mr. Paul Ward, director of the California Committee on Regional Medical Programs, reported on progress under Public Law 89-239. He said that the major problem facing the programs is misunderstanding because the means of implementation have changed drastically since the "DeBakey Report" was first issued. Mr. Ward said that by Congressional intent the key to success of these programs is synthesis—the local involvement of many groups and individuals before concepts are developed (as opposed to programs for which plans are handed down "from the top"). Mr. Ward asked for CMA help in reaching local physicians and other health professionals in areas outside of metropolitan centers so that these persons may become actively involved in the planning process.

On behalf of the Advisory Committee to CMA Representatives on the California Committee on Regional Medical Programs, Councilor Malcolm S. M. Watts presented four recommendations for Council consideration: (a) that California continue to be designated a region with sub-areas, (b) that the program in each sub-area be structured to meet its particular needs, (c) that CMA publicize its support of this program, and (d) that CMA inform local physicians concerning the nature of the program, encouraging them to participate in the development.

ACTION: *Voted to approve the above recommendations concerning California implementation of P. L. 89-239.*

21. *California Delegation to the AMA*

Doctor Eugene F. Hoffman, Sr., chairman of the CMA Delegation to the AMA, reported on the activities and accomplishments of the Delegation at the recent AMA Convention in Atlantic City. Doctor Hoffman first expressed the pride of all California physicians in the unanimous election of Doctor Dwight L. Wilbur to be AMA President-Elect and the election of Doctor Burt Davis as Trustee to the Board. Doctor Hoffman paid tribute to every member of the Delegation for his endeavors and pointed out that 15 of the 19 CMA resolutions were adopted and one referred for further consideration. Of the three remaining, one

resolution was substantially changed and only two were not adopted.

He also commented on the pleasure of the Delegation at having a number of executive secretaries join them at caucuses and said that this was a break with tradition which was long overdue.

Rather than go into a summary of actions taken at the convention, Doctor Hoffman referred the Council to AMA reports. He stated, however, that the House had voted to authorize the Board of Trustees to continue the disability insurance program with the same level of benefits and at the same premium, that it fully supported efforts to hasten the conversion of schools of osteopathy to schools of medicine, and that it took a position on therapeutic abortion similar to that taken by CMA.

Doctor Hoffman said that he, as newly-elected chairman of the Delegation, and Doctor Sam Sherman, as vice-chairman, would make every effort to deserve the confidence of the CMA. In conclusion, Doctor Hoffman congratulated CMA staff members for their dedication and devotion to the work of the Delegation.

22. *Bureau of Research and Planning*

Doctor Carl E. Anderson, chairman of the Bureau, reported that at its 7 June 1967 meeting, the subject of goals and functions for the Bureau of Research and Planning received considerable attention. Doctor Anderson presented the following as recommended *functions* of the Bureau:

1. By utilizing research capabilities of the Bureau, to provide informational service and advice to the various committees of the Association, as well as to component medical societies and to individual physicians.

2. To initiate fact-finding and analytical studies and creative programs in order to enhance the effectiveness of all segments of the Association, and

3. To report on studies and findings of other groups and individuals as they may be of interest to, or have a bearing on, the objectives and goals of the medical profession.

ACTION: *Voted to approve the above as functions of the Bureau of Research and Planning.*

Doctor Anderson also commented briefly on two major surveys under way for the Committee on Continuing Medical Education, under an NIH grant to CMERF (on behalf of the California

Committee on Regional Medical Programs). One was described as a questionnaire survey among 5,000 physicians to secure their opinions, attitudes and suggestions regarding continuing medical education; the other, as a census study of all courses and physicians who either give or take them. Doctor Anderson said that medical schools and their local cooperative arrangements are eagerly awaiting results for further planning purposes.

Regarding financial support for CMA studies, Doctor Anderson reported that an effort had been made to determine whether support of private foundations could be obtained. Contacts with several foundations corroborated previous advice to the Bureau that private foundations are not interested in going into areas of research or study where the Federal government has made a considerable commitment.

Doctor Anderson also reported the Bureau's progress on two resolutions of the 1967 CMA House of Delegates: Numbers 9 (Quality of Medical Care) and 44 (Utilization Study of Closed Panel Plans).

23. *Committee on Legislation*

Chairman Dan O. Kilroy informed the Council that the State Legislature appears to be headed for its final month. He said that although the session started off slowly, the tempo has increased markedly in the last 60 days, with many items of interest to medicine. Doctor Kilroy reviewed those bills on which there had been some action.

The Council and medical executives were reminded that Public Health League staff would be visiting component societies this fall to report on legislative activities affecting medicine.

24. *Conference with Representatives of Specialty Societies*

In the absence of Chairman Glenn A. Pope, Councilor Kaiser, a member of the ad hoc Committee on Medical Specialty Conference, drew the attention of the Council to the proposed format for the Conference, to be held 7 October 1967 at the Hilton Inn, San Francisco.

Councilor Kaiser expressed confidence on behalf of the committee that this Conference would serve as an excellent device to begin building better relationships between medical specialty organizations and the CMA. He asked that the Council designate two of its members to serve as resource persons for each of the five discussion groups at the Conference.

25. *Commission on Community Health Services*

Chairman Harold Kay commented briefly on progress of the Health Manpower Council, which had recently held two meetings, still organizational in nature. Doctor Kay also remarked on the multiphasic screening program for cannery workers being conducted by the Health Testing Services, Inc. Doctor Kay said that the Commission recommended that CMA neither approve nor disapprove of this particular program and that if similar projects are initiated in the future, county medical societies should be involved during the early planning stages.

Doctor Kay announced that Wayne P. Chesbro had been elected vice-chairman of the Commission.

He also drew attention of the Council to changes in the Health and Safety Code pertaining to blood banks, pointing out that sections 998(b) and 1002(d) under which regulations relating to blood banks are operative, prescribe that the attending physician shall provide direct and "responsible" (rather than "immediate") supervision of the bleeding of donors. On behalf of the Committee on Blood Banks and the Commission, Doctor Kay recommended CMA concurrence with the changes in the regulations.

ACTION: *Voted to concur with changes in the Health and Safety Code pertaining to blood banks which would eliminate the necessity of a physician being in immediate attendance, and call instead for responsible supervision by a licensed physician.*

Doctor Kay said that this action satisfied House of Delegates Resolution No. 61-67 (Medical Supervision of Blood Banking During Unscheduled Emergency Blood Collections).

Doctor Kay announced that the AMA Council on Rural Health is considering holding its 1971 Annual Conference in California. On behalf of the Committee on Rural Health and the Commission, he recommended that CMA extend an appropriate invitation to the AMA.

ACTION: *Voted to approve extending an invitation to the AMA Council on Rural Health to hold its 1971 conference in California.*

Doctor Kay recommended, on behalf of the Committee on School and College Health, that it establish liaison with the American School Health Association.

ACTION: *Voted to approve the establishment of liaison with the American School Health Association.*

Doctor Kay discussed a proposed "Clinical Laboratory Proficiency Testing Program" and asked

for Council permission to continue to work with the California Society of Pathologists, the California Association of Clinical Laboratories, the California Society of Internal Medicine and the State Department of Public Health in working out a plan of participation in such a program for clinical laboratories.

ACTION: *Voted to authorize the Commission on Community Health Services to continue working with designated organizations on developing a program of proficiency testing for clinical laboratories.*

As the last item in his presentation, Doctor Kay recommended to the Council that it appoint Doctor Charles Baker of Oakland to serve as a "CMA reporter" on the Cytology Testing Subcommittee of the State Department of Public Health.

ACTION: *Voted to appoint Doctor Charles Baker to serve as "CMA Reporter" on the SDPH Cytology Testing Subcommittee.*

26. 26 August Meeting of Council

After some discussion about possible conflict between the AMA Communications Institute and a meeting of the Association of State Society Presidents with the 26 August 1967 meeting of the Council, the following decision was made:

ACTION: *Voted to stay with the previously scheduled date of 26 August for the next meeting of the CMA Council.*

27. Committee on Organizational Review and Planning

Doctor Jean Crum, chairman, briefly discussed subjects with which the committee is currently concerned, but is recommending no definite action at this time, including: (1) physician manpower needs in California, (2) study of the function of the previous Committee on Scientific Information, (3) committee objectives for the year (stressing the functional structure of the Association), and (4) House of Delegates Resolution 30-67 (Delegates, Limitation of Continuous Terms). On the last item, Doctor Crum pointed out that the committee felt that the problem of continuous terms for Delegates and Alternates to the CMA is one over which each District exercises local control through the process of election. He said that the record of service of the AMA Delegates and Alternates is being researched.

On behalf of the committee, Councilor Crum asked for Council approval of three recommendations, with the following results:

ACTION: *Voted to authorize the Committee for Emergency Action to designate individuals to assist as the need arises in the 1968 meeting of the National Health Council in Los Angeles (topic of the meeting is Quality in Health Care).*

ACTION: *Voted to urge Component Society Officers and Executive Secretaries to begin serious consideration of Component Society and CMA goals.*

ACTION: *Voted to establish a task force on P. L. 89-749 (Comprehensive Health Planning) charged with the responsibility to lead and to involve the profession in California.*

28. California Blue Shield

Blue Shield Board Chairman Richard S. Wilbur discussed the "Major Medicare" campaign now underway, stating that the open enrollment period will extend through 31 August 1967. Doctor Wilbur emphasized that Blue Shield is not only offering this program, designed to supplement Medicare, but is continuing to offer health protection plans to those over 65 who are not enrolled in Medicare.

Doctor Wilbur also displayed and explained a chart showing expenditures under Medi-Cal—actual expenditures from 1 May 1966 to 30 April 1967, which have been reported to the intermediaries and estimated expenditures for the fiscal year 1967-68. He pointed out that one of the most significant aspects of the chart is that while total expenditures are expected to increase substantially, the percentage of the total cost represented by physician services is expected to decrease.

ACTION: *Voted to request the CMA Commission on Communications to consider publicizing the chart, when a refined version is received from Blue Shield.*

29. Commission on Allied Health Professions and Services

Chairman Frank Melone reported that at the 28 June meeting of the Commission, Doctor Thomas W. Ledwich of Napa had been elected vice-chairman.

Doctor Melone also reported on House of Delegates Resolution No. 26-67 (Nurse-Midwife Training Program). He said that the Commission had reviewed earlier deliberations of the Committee on Other Professions concerning nurse obstetrical assistants and midwifery. This committee had expressed the idea that if a need exists in obstetrics, it also probably exists in other areas of medicine. Thus, the committee favored developing a program to attract physicians to geographic areas of need as a more realistic solution. Doctor Melone

said that this position was reaffirmed by the Commission, which recommended that further study be given to the matter by the Committee on Maternal and Child Care—as called for by Resolution 26-67. The Commission asked that findings from this study be made available to the Commission for its review and further consideration.

On behalf of the Commission, Councilor Melone recommended that the name of the Committee on Paramedical Personnel be changed to the “Committee on Allied Health Personnel.”

ACTION: *Voted to authorize changing the name of the Committee on Paramedical Personnel to “Committee on Allied Health Personnel.”*

30. *Report of the Scientific Board*

Chairman Longmire gave an informal preliminary report on progress of the Scientific Board in formulating recommended CMA policy in two areas of vital concern: CMA’s role in chronic disease control and CMA’s financial support for the Tumor Tissue Registry. Doctor Longmire said that recommendations on each of these subjects would be presented to the Council in written form in the near future.

31. *Report of the Commission on Hospital Affairs*

Chairman MacLaggan discussed progress of the hospital Medical Staff Survey program. He also stated that Doctor Arthur Rice of Alameda-Contra Costa Medical Association had recently reported on promising new method of standardizing hospital medical records. Doctor MacLaggan recommended that an ad hoc committee be appointed to explore new methodology in standardization (with Doctor Rice).

ACTION: *Voted to establish an ad hoc Committee to Study Standardization of Hospital Medical Records (to be nominated by the Committee on Committees).*

32. *Subcommittee on Long-Term Care Facilities*

Chairman Kaiser reported that the subcommittee unanimously agreed to ask Council permission to undertake a study of extended care facilities in a certain geographic area (types of patients, types of facilities, gradations of care etc.). It was pointed out that a Federal grant would have to be sought for this project, which would be done in cooperation with the Bureau of Research and Planning.

ACTION: *Voted to authorize the Subcommittee on Long-term Care Facilities to proceed with plans for federally financed study of extended care facilities*

(in cooperation with the Bureau of Research and Planning).

33. *Report of the Medical Executives Conference*

Mr. Eldon Geisert, chairman of the Medical Executives Conference, gave highlights of the previous day’s meeting, stressing the strong feeling of the medical executives regarding the need for telling the positive side of the story of physician participation in government programs—particularly Medi-Cal and Medicare. Mr. Geisert also reported that the MEC is extremely concerned with the problem of malpractice insurance. He reported to the Council that six new members had been nominated for submission to the Council for its approval.

ACTION: *Voted to approve the following as new members of the Medical Executives Conference: Curt Searcy of Napa, John Hirsimaki of Santa Clara, Dick Church of San Joaquin, Paul Humbert of Fresno, Bob Gillies of Sacramento, and Jim Webb of Kern.*

Mr. Geisert called on Mr. Clark Donmyer, chairman of the MEC Subcommittee on P. L. 89-749 (Comprehensive Health Planning). Mr. Donmyer referred to a written report which had been distributed to the Council, containing recommendations that:

a. Each component medical society take the initiative in forming local Health Planning Councils, patterned after the State Health Planning Council.

b. Such local Health Planning groups which are representative of the community take immediate steps to inventory and assess their total community environmental and personal health needs.

c. On the basis of such determination specific Health Planning Goals be established as steps to be taken to develop specific programs to alleviate or correct existing problems, or to anticipate future ones.

d. At suitable intervals such programs be evaluated to determine the effectiveness of the programs which have been developed.

e. The comprehensive health planning activities be revised at periodic intervals in order to establish new goals and programs when necessary.

ACTION: *Voted to approve the above recommendations for referral to the newly established Task Force on P. L. 89-749 for implementation.*

34. *Scheduling of Future Annual Sessions*

Mr. Howard Hassard reported that since the Council action authorizing staff planning for An-

nual Sessions for the coming five years, the following times and locations have been set: 1968—March 23-27 at the Fairmont and Mark Hopkins Hotels, San Francisco; 1969—March 15-19 at the Ambassador Hotel, Los Angeles; 1970—March 7-11 at the Hilton Hotel, San Francisco.

Mr. Hassard said that after 1970, it is expected that the Century Plaza Hotel in Los Angeles will have added enough meeting rooms and exhibit space to accommodate the CMA Annual Session, and that some time after 1971 sites in Anaheim and San Diego may be sufficiently developed so that they can be considered.

35. *Report of Legal Counsel*

Legal Counsel Hassard reported that in the field of malpractice, the inflationary trend has taken another boost upward. He cited several recent court decisions which indicate an unmistakable fact—that the cost to California physicians of insuring for professional liability is going up substantially.

Mr. Hassard also commented on a pending case involving medical staff privileges. He said that the decision on this case would probably establish rules which will be applicable regardless of the nature of the hospital.

36. *Membership*

On recommendation of Orange County Medical Association, Michael J. DeLuca, M.D., was reinstated as an active member.

Fifteen applicants were voted election to Associate Membership: Floyd P. Paudle, Alameda-Contra Costa County; J. Richard R. Bobb, Alonzo Cass, Donald O. Costley, John H. Morton, Howard Lawrence Rosenfeld, Los Angeles County; George L. Beatty, James Ownby, Napa County; Paul A. Bendix, Riverside County; John A. Ariando, San Bernardino County; Gilbert E. Kinyon, San Diego County; Olav N. Norman, San Francisco County; Yale Brody, San Joaquin County; Ralph Thomas Duddles, Santa Barbara County; Fred R. Lewis, Sonoma County.

Nine members were voted election to Retired Membership: Elmer J. Schmidt, Fresno County; Carroll A. McCoy, Los Angeles County; Clifford P. McCullough, Riverside County; Christopher Leggo, Sacramento County; Ruth L. Green, H. C. Mathews, San Bernardino County; Herbert W. Meyer, San Diego County; Garnett W. Hooker,

San Joaquin County; E. Dwight Barnett, Santa Clara County.

Reduction of dues was voted for 15 members for reasons of prolonged illness or postgraduate education.

37. *Roll Call*

Present were President Morrison, President-Elect Todd, Speaker Quinn, Vice-Speaker Boyle, Secretary Weyrauch and Councilors Moore, Melone, Eastman, Woolington, Gooel, Pheasant, Bullock, O'Connor, Shapiro, Rogers, Crum, Watson, Maguire, Burnett, Richard Wilbur, Miller, Watts, Fenlon, Kay, Kaiser, Rose, Yant, Grunigen, Longmire and Immediate Past President MacLaggan.

Present by invitation were CMA staff members Becker, Bowman, E. Collins, J. Collins, Curley, Eberlein, Goldman, Griffith, Hetland, Jones, Klutch, Lemos, Miller, Price, Redfern, Thomas and Whelan; Messrs. Hassard and Huber, Legal Counsel, component society executives Scheuber of Alameda-Contra Costa, Rideout of Butte-Glenn, Garrick of Forty First, Lingerfelt of Fresno, Geisert of Kern, Brock of Imperial, Dalbec of Los Angeles, Sower of Marin, Colvin of Monterey, Walters of Riverside, Dochterman of Sacramento, Donmyer of San Bernardino, Nute of San Diego, Neick of San Francisco, Thompson of San Joaquin, Wood of San Mateo, Marvin of Santa Barbara, Donovan of Santa Clara, Brown of Sonoma and Bruce of Tulare; Messrs. Paton, Babb, Clark and Koch of California Blue Shield; Messrs. Read, Brown and Putnam of the Public Health League; medical school representatives Doctor Gonda of Stanford, Doctor Bauer of USC, Doctor Bostick of UC-CCM and Doctor Dillon of UCLA; Doctor Goerke of UCLA School of Public Health; Messrs. Williams and Rosen of the State Health and Welfare Agency; Doctor Breslow of the State Department of Public Health; Doctor Young of the State Department of Rehabilitation; Doctor Skelly of the State Department of Social Welfare; Doctor Nash of Camarillo State Hospital; Mrs. Kahn of the Bureau of Health Insurance, Social Security Administration; Mr. Ward and Doctor Epstein of the California Committee on Regional Medical Programs; Messrs. Gates and Gould of the AMA; Doctor Maeda of the California Veterinary Medical Association; Mrs. Flood of the Woman's Auxiliary to the CMA; Mrs. Hancock of the California Nurses' Association; Miss Goldman of the California Medical Assistants Association; Mr. Moore of the American Hospital Association; Doctors

Anderson, Elliott, Felt, Hoffman, Judd, Kilroy, Steinberg, Steinmetz and others.

38. Adjournment

The meeting was adjourned on Saturday, 8 July, at 4:45 p.m.

ALBERT G. MILLER, M.D., *Chairman*

HELEN B. WEYRAUCH, M.D., *Secretary*

535th Meeting

Tentative Draft: 535th Meeting of the Council, Los Angeles, Airport-Marina Hotel, 2 August 1967.

The meeting was called to order by Chairman Miller at the Airport-Marina Hotel near Los Angeles on Wednesday, 2 August 1967, at 8:30 p.m.

A quorum was present and acting (full roll call, including names of invited guests, appears in Item II).

Purpose of this special meeting of the Council was described as being to consider current developments regarding the Medi-Cal program and its fiscal status.

I. Chairman Miller called upon President Morrison to initiate discussion on current Medi-Cal problems and their possible solutions. The in-depth discussion which ensued included a presentation by Carel E. H. Mulder, director of the Office of Health Care Services.

After due consideration of the issues involved in Medi-Cal fiscal problems, the Council:

ACTION: *Voted to endorse the concept of placing selective controls on the small percentage of physicians who deviate from accepted patterns with regard to Medi-Cal and to request the Office of Health Care Services to make the names of such physicians available to CMA and the appropriate component societies so that designated local committees can review and act upon these cases.*

ACTION: *Voted to authorize the president of CMA and the president of the Los Angeles County Medical Association to appear at a press conference to be held on Thursday, 3 August, to inform the public*

that the basis for Medi-Cal fiscal problems lies in areas other than physician fees, and that California physicians have been actively involved in helping to provide quality care at reasonable costs under Medi-Cal and to suggest constructive actions that might be taken to alleviate fiscal difficulties under the program.

ACTION: *Voted to approve suggestions for curbing Medi-Cal costs through better utilization control methods, including, but not limited to: (a) eliminating items not medically required, (b) placing selected controls on some medical procedures, and (c) encouraging patient responsibility, possibly through a co-insurance feature. These suggestions were endorsed as acceptable alternatives to cost-cutting measures which would impair patient care (e.g. establishing a county hospital corridor for all hospitalization, discouraging physician participation through imposition of a fee schedule).*

II. Roll Call

Present were President Morrison, President-Elect Todd, Speaker Quinn, Vice-Speaker Boyle, Secretary Weyrauch, and Councilors Moore, Eastman, Woolington, Gooel, Shapiro, Bullock, O'Connor, Pheasant, Rogers, Crum, Maguire, Burnett, Richard Wilbur, Miller, Watts, Fenlon, Kay, Kaiser, Rose, Yant, Grunigen and Immediate Past President MacLaggan.

Present by invitation were CMA staff members, E. Collins, Curley, Eberlein, Klutch, Lemos, Price, Redfern, Thomas and Whelan; Legal Counsel Willett; component society executives Scheuber of Alameda-Contra Costa, Lingerfelt of Fresno, Brock of Imperial, Geisert of Kern, Dalbec of Los Angeles, Sower of Marin, Colvin of Monterey, Blough of Orange, Walters of Riverside, Dochterman of Sacramento, Donmyer of San Bernardino, Nute of San Diego, Neick of San Francisco, Wood of San Mateo, Marvin of Santa Barbara, Donovan of Santa Clara, McGowan of Sonoma and Whitehall of Stanislaus; Messrs. Read and Brown of the Public Health League; Messrs. Babb, Clark, Heller, Koch and Potloff of California Blue Shield; Mr. Mulder of the Office of Health Care Services, Mr. Shumway of the Health and Welfare Agency; Doctors Anderson, Howard, Lindsey and others.

Adjournment

The meeting was adjourned at 11:10 p.m.

ALBERT G. MILLER, M.D., *Chairman*

HELEN B. WEYRAUCH, M.D., *Secretary*

In Memoriam

AGINS, JACOB, Los Angeles. Died 7 July 1967 in Los Angeles of carcinoma of the colon, aged 69. Graduate of Wayne University College of Medicine, Detroit, 1925. Licensed in California in 1945. Doctor Agins was a member of the Los Angeles County Medical Association.



BERMAN, JOHN A., Oakland. Died 7 August 1967 in Monterey, aged 35. Graduate of University of Minnesota Medical School, Minneapolis, 1957. Licensed in California in 1958. Doctor Berman was a member of the Alameda-Contra Costa Medical Association.



BERNHARD, RUSSELL WILLIAM, San Rafael. Died 28 July 1967 in San Rafael, aged 54. Graduate of the University of Cincinnati College of Medicine, 1938. Licensed in California in 1943. Doctor Bernhard was a member of the Marin County Medical Society.



BUTKA, HERSEL E., Placerville. Died 11 May 1967, aged 72. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1917. Licensed in California in 1917. Doctor Butka was a member of the Sacramento County Medical Society.



CRITES, ALBERT H., Port Hueneme. Died 7 August 1967, aged 65. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1943. Licensed in California in 1943. Doctor Crites was a member of the Ventura County Medical Society.



DAVIS, RUFUS A., Palm Desert. Died 29 June 1967 in Long Beach of carcinoma of the colon, aged 62. Graduate of College of Osteopathic Physicians and Surgeons, Los Angeles, 1928. Licensed in California in 1928. M.D. degree from California College of Medicine in 1962. Doctor Davis was a retired member of the Los Angeles County Medical Association and the California Medical Association and an associate member of the American Medical Association.



GREEN, RUTH L., San Bernardino. Died 25 June 1967, aged 58. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1934. Licensed in California in 1935. Doctor Green was a retired member of the San Bernardino Medical Society and the California Medical Association, and an associate member of the American Medical Association.



HARE, HUGH FREDERICK, Los Angeles. Died 17 July 1967, aged 65. Graduate of Harvard Medical School, Boston, Massachusetts, 1928. Licensed in California in 1953. Doctor Hare was a member of the Los Angeles County Medical Association.



IRISH, CULLEN WARD, Los Angeles. Died 23 July 1967 in Los Angeles of arteriosclerotic disease, aged 77. Graduate of Ohio State University College of Medicine,

Columbus, 1915. Licensed in California in 1931. Doctor Irish was a retired member of the Los Angeles County Medical Association and the California Medical Association, and an associate member of the American Medical Association.



KARSANT, SABRA JAMES, San Francisco. Died in San Francisco 2 August 1967 of heart disease, aged 49. Graduate of the University of California Medical School, San Francisco, 1944. Licensed in California in 1945. Doctor Karsant was a member of the San Francisco Medical Society.



MILLITZER, MARIAN MONICA, Pasadena. Died 6 July 1967 in Pasadena of heart disease, aged 56. Graduate of Loyola University School of Medicine, Chicago, Illinois, 1937. Licensed in California in 1937. Doctor Millitzer was a retired member of the Los Angeles County Medical Association and the California Medical Association, and an associate member of the American Medical Association.



O'NEILL, JOHN R., San Francisco. Died 11 July 1967 in San Francisco of coronary artery disease, aged 70. Graduate of St. Louis University School of Medicine, 1920. Licensed in California in 1921. Doctor O'Neill was a member of the San Francisco Medical Society.



PAGE, BENJAMIN H., San Mateo. Died 2 July 1967 in San Mateo, aged 75. Graduate of Stanford University School of Medicine, Palo Alto-San Francisco, 1926. Licensed in California in 1926. Doctor Page was a retired member of the San Mateo County Medical Society and the California Medical Association, and an associate member of the American Medical Association.



PREMO, MILTON ALEXANDER, San Jose. Died 3 August 1967 in Santa Clara, aged 65. Graduate of Creighton University School of Medicine, Omaha, Nebraska, 1929. Licensed in California in 1930. Doctor Premo was a retired member of the Santa Clara County Medical Society and the California Medical Association, and an associate member of the American Medical Association.



RICHARDS, ROBERT ARTHUR, Rolling Hills. Died 4 July 1967, aged 51. Graduate of New York University College of Medicine, New York City, 1944. Licensed in California in 1950. Doctor Richards was a member of the Los Angeles County Medical Association.



SHILLING, JEROME WARREN, Los Angeles. Died 27 July 1967 in Los Angeles of carcinomatosis, aged 69. Graduate of Washington University School of Medicine, St. Louis, Missouri, 1924. Licensed in California in 1926. Doctor Shilling was a retired member of the Los Angeles County Medical Association and the California Medical Association, and an associate member of the American Medical Association.

SKOLNICK, EDWARD AISIK, Los Angeles. Died 4 July 1967 in Culver City of myelogenous leukemia, aged 80. Graduate of Loyola University School of Medicine, Chicago, Illinois, 1913. Licensed in California in 1959. Doctor Skolnick was a member of the Los Angeles County Medical Association.

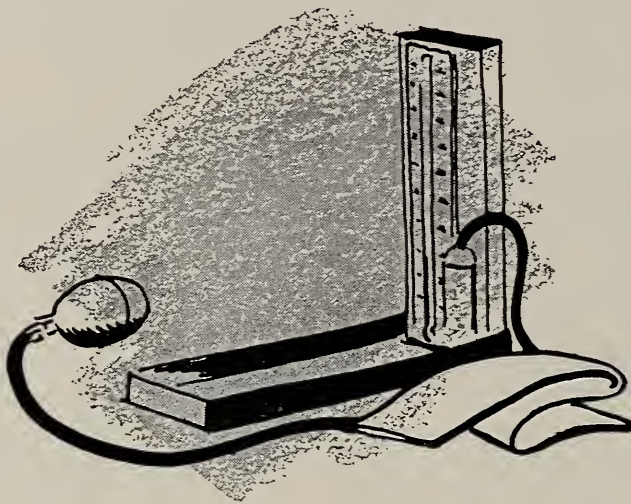


VAN DER HEIDE, CAREL, Beverly Hills. Died 17 April 1967 in Santa Monica of renal shut down, aged 62. Graduate of Universiteit van Amsterdam Geneeskunde Faculteit, Amsterdam, The Netherlands, 1930. Licensed

in California in 1947. Doctor Van der Heide was a member of the Los Angeles County Medical Association.



WATSON, HAROLD G., San Francisco. Died 6 August 1967 in Carson City, Nevada, aged 65. Graduate of University of California Medical School, Berkeley-San Francisco, 1932. Licensed in California in 1932. Doctor Watson was a retired member of the San Francisco Medical Society and the California Medical Association, and an associate member of the American Medical Association.



Planning and Goals Conference in Continuing Medical Education

Workshop Recommendations

Including Modifications Recommended by the Entire Conference and by the Scientific Board at Its Meeting, 1 April 1967

■ *Following are recommendations drawn up by workshops held as a part of the Planning and Goals Conference in Continuing Medical Education, sponsored by the California Medical Association and directed by its Committee on Continuing Medical Education, San Diego, 11 to 12 March 1967. The general subject was divided among four workshops and the reports of two of them—No. 1, (a) and (b), and No. 2—were printed in the August issue of CALIFORNIA MEDICINE. The Reports herewith are those of the other two workshops.*

The conference was supported in part by Contract No. PH 108-67-158, Bureau of Health Manpower, Public Health Service, Department of Health, Education and Welfare.

Motivation

Report of Workshop 3

Discussion Leader—John B. Dillon, M.D.

Secretary—Robert Combs, M.D.

Panelists—Joseph Boyle, M.D., and
Saul Robinson, M.D.

CONFERENCE WORKSHOP #3 was charged to study the problem of motivation and make specific recommendations. The workshop seemed to be of interest, was well attended, kept its group involved, intense and frequently heated discussion.

The group considered whether motivation for continuing education was in fact needed. There was no factual data available as to the total number of California physicians not engaged in continuing educational effort and it was hoped that ongoing studies by CMA's Committee on Continuing Medical Education in cooperation with the California Medical Education and Research Foundation would have information in the near future. It was agreed that although the problem could not be quantitated that it did exist and probably was of sufficient magnitude to justify serious study and remedial effort.

The group agreed that continuing educational effort is essential for all practicing physicians and considerable discussion took place suggesting reasons why physicians might not actively engage in such effort. It was recognized that there are probably numbers of physicians who engage in educational activities in private, that is read and study extensively but do not partake of or engage in any organized group study or attend meetings, seminars or professional societies.

The present image of the physician was discussed particularly in reference to the "Millis Report" and present social legislation. It was generally agreed that as medical facilities were being looked at as to quality, it was only a matter of time until the quality of professional care would be looked at in the same way. There have been suggestions along this line already by Doctor James, former New York Commissioner of Health.

An extensive discussion developed around the topic of mechanisms to demonstrate evidence of continued educational effort and an acceptable level of continued competence. It was agreed that the medical profession itself should set standards

and avoid, in so far as possible, any intervention of government at any level. It was recognized that such evidence of continued education would be in the physician's area of special interest. The format of the Academy of General Practice was discussed and the group was advised that a similar format was being considered for the developing specialty of the "Primary Physician."

It was generally agreed that logistics precluded re-examination not only by a State Board but by specialty groups. The number of physicians involved would be so great as to make such procedures impractical.

It was agreed after consideration discussion that some objective evidence of continuing education is desirable as like Caesar's wife "One must appear to be above reproach." It was further agreed that each specialty group would probably be in the best position to determine the requirements for continuing approval. There was discussion and general agreement that the CMA should encourage various groups to study the problems of continuing education as it pertained to them. No specific recommendations were suggested as the methods would be perhaps as numerous as the numbers of specialties involved.

There was heated and prolonged discussion on the implications of the word motivation. Several believed that there should be compulsory requirements with definite penalties for failure to comply. The majority believed that any requirements should be voluntary, that is, failure to show evidence of continued medical education would not result in cancellation of licensure but would result in the physician not having whatever evidence of continued educational effort it was decided ultimately would be appropriate. It was believed that those physicians who did not comply would not receive a certificate, for example, which would exert sufficient moral persuasion to, in time, produce the desired results.

It was agreed that if such an educational effort were fostered by the CMA officially that this would indeed show evidence of the interest by "medicine" in maintaining standards over training and keeping its educational house in order.

On the basis of the above discussion the group as a whole formulated the following resolutions for consideration by the Scientific Board with the idea of possible referral to the House of Delegates of the CMA after proper channeling.

The Workshop recommended:

1. That the CMA Council institute a study of certification and recertification of physicians at suitable intervals, as a means of encouraging all California physicians to continue their medical education, and

2. That there be investigated means whereby the teaching community be more closely integrated with the physician community as a whole, and

It was further recommended:

3. That an ongoing research project in continuing education be directed to study the reasons for the apparent lack of participation by certain segments of California physicians in formal post-graduate education.

The group appreciated the counsel of Doctor Edward Shaw, former Chairman of the Scientific Board.

Personnel of Workshop 3

Discussion Leader—John B. Dillon, M.D., Los Angeles, Member, CMA Committee on Continuing Medical Education; Professor of Surgery/Anesthesiology and Assistant Dean, University of California, Los Angeles, School of Medicine.

Secretary—Robert Combs, M.D., San Francisco, President, Board of Medical Examiners, State of California.

Participants:

Leland B. Blanchard, M.D., San Jose, Member, CMA Scientific Board

Joseph F. Boyle, M.D., Los Angeles, CMA Councilor; President, Los Angeles County Medical Association; Associate Clinical Professor of Medicine, University of Southern California School of Medicine

Arthur A. Clinco, M.D., Los Angeles, Member, CMA Scientific Board; Associate Professor of Psychiatry, University of California, Los Angeles, School of Medicine

W. Philip Corr, M.D., Riverside, Governor, Southern California Region, American College of Physicians

Roberta Fenlon, M.D., San Francisco, CMA Councilor; Member, CMA Commission on Communications

Charles E. Grayson, M.D., Sacramento, Member, CMA Committee on Continuing Medical Education

Lester T. Hibbard, M.D., Los Angeles, Chairman, CMA Section on Obstetrics and Gynecology

A. F. Kandlbinder, M.D., Monterey, District Representative to the CMA Committee on Continuing Medical Education

Richard Opfell, M.D., Santa Ana, Co-Chairman, Orange County Medical Association Continuing Medical Education Committee

Saul J. Robinson, M.D., San Francisco, Member, CMA Committee on Continuing Medical Education

Edward S. Rogers, M.D., Berkeley, University of California, Berkeley, School of Public Health

Morton K. Rubenstein, M.D., Los Angeles, Assistant Professor of Neurology, University of California, Los Angeles, School of Medicine

John T. Saidy, M.D., San Mateo, Member, CMA Committee on Organizational Review and Planning; CMA Medical Staff Survey Committee

Edward Shanbrom, M.D., Santa Ana, District Repre-

sentative to the CMA Committee on Continuing Medical Education

Edward B. Shaw, M.D., San Francisco, Member and Former Chairman, CMA Scientific Board; Formerly Professor and Chairman, Department of Pediatrics, University of California, San Francisco, School of Medicine

Wilfred Snodgrass, M.D., San Francisco, Chairman, Education Committee, California Academy of General Practice

Henry Zevely, M.D., San Luis Obispo, Chairman, Postgraduate Activities Committee, San Luis Obispo County Medical Society

Accreditation or Approval of Courses or Programs in Continuing Medical Education

Report of Workshop 4

Discussion Leader—Arthur Selzer, M.D.

Secretary—Charles J. Tupper, M.D.

Panelists—Donald Brayton, M.D., and Robert S. Quinn, M.D.

THE CHARGE to the workshop was a review of the need for a program of accreditation of postgraduate courses and a recommendation as to the initiation of such a program if the need for it was established.

The meeting was opened by introducing two representatives of the AMA's new Department of Continuing Medical Education. The director of this department, Doctor William Ruhe, was unable to attend our meeting because of a conflicting committee meeting in Chicago. Representing him were Doctor William Sullivan and Doctor Glen Shepherd. Doctor Shepherd reviewed the history of the AMA's efforts to develop a regulatory program for continuing medical education. Several years of study culminated in a plan to accredit institutional programs, rather than individual courses. This plan was tested by a series of site visits to some postgraduate institutions in 1963 and 1964, but was then temporarily dropped. In February 1967 the AMA officially committed itself to the accreditation program and decided that the format proposed in 1964 should be adopted.

The group discussed the problem of accreditation as applied specifically to California. It was felt that the chaotic situation that exists in the field of postgraduate courses would be greatly improved if a regulatory mechanism were introduced. It was the unanimous feeling of the group that a program of certification or accreditation of postgraduate activities is very desirable for California and the

CMA is the logical organization to take the lead in instituting such a program. It was also agreed that accreditation of individual courses is totally impractical and the AMA plan of accrediting institutions which offer such programs is the best approach to this problem. The criteria of excellence for such an accreditation program were briefly discussed and it was felt that the AMA has done an admirable job in establishing such criteria, summarized in its publication, "Guide Regarding Objectives and Basic Principles of Continuing Medical Education," and that the AMA criteria should be officially adopted for California.

In the discussion the question was brought out as to whether a state accreditation program would create duplication of the existing AMA program. It was the feeling of the group, as well as of the AMA representative, that this would not be the case if a proper liaison were arranged between the respective committees of the two organizations. It was thought likely that the AMA—facing a huge task of national accreditation—might rely heavily on the work of the California committee.

A detailed discussion of the proposal by Doctor Brayton to designate a group of institutions which would be automatically accredited under a "grandfather clause" revealed a wide divergence of opinion. The final consensus, including that of Doctor Brayton, was that there should be no automatic accreditation of any institution in the state.

The workshop then addressed itself to the need to start with a review committee and suggested that the review committee be protected from political domination. A formal action was taken to recommend to the CMA Council to charge the Scientific Board with the responsibility to appoint a committee, "Committee on Accreditation of Programs in Continuing Medical Education," which should be responsible to the Scientific Board. A good deal of discussion dealt with the composition of the committee. It was agreed that this workshop should provide general guidelines for the composition of the committee, but should not recommend a specific number of members, leaving this to the Scientific Board. It was felt that the liaison with the AMA is of considerable importance and some mechanism should be explored to have overlapping membership of the respective AMA and CMA committees dealing with continuing medical education accreditation. Inasmuch as many of the voluntary health agencies are engaged in the organization and support of postgraduate courses, the advisability of their representation on

the committee was discussed, but the consensus was that a liaison with such agencies be established rather than to recommend an obligatory representation on the committee.

In the discussion it was emphasized that the committee should have a broad base and wide representation as a prerequisite of its effective operation. The final recommendation of the group was to invite nominations to the committee from the following: (1) The medical schools, (2) the California Hospital Association—as a means to represent hospital directors of medical education, (3) the State Health Department (the plenary session on March 12 changed this recommendation to read “an appropriate state agency”). A broad-based committee drawn from the membership of the CMA should include representation from the California Academy of General Practice and the various specialty groups.

The discussion further stressed the need for providing continuity on the committee. It was also felt that the committee should include physicians who would be “consumers” of continuing medical education as well as those whose responsibility is to organize the courses.

The discussion briefly touched upon the problem of evaluation of postgraduate teaching—a subject taken up by another workshop. The opinion was expressed that accreditation and evaluation are part and parcel of one another, especially since certification is visualized as a repetitive and continuous process.

In summary, the workshop recommends:

1. Accreditation is desirable.
2. Acceptance and endorsement of the AMA “Guide” as a statement of basic principles.
3. Formation of a California Committee on Accreditation Programs in Continuing Medical Education.
4. Organization of the committee under CMA’s Scientific Board, the committee to be chaired by a member of the Scientific Board.
5. Representation from:
 - a. Medical Schools.
 - b. The California Hospital Association—as a means to represent hospital directors of medical education.
 - c. An appropriate State agency.
6. Appointment of CMA members as physicians at large, including the representatives of the California Academy of General Practice and some

of the various specialty groups, including Public Health.

The committee further recommends that active liaison with the AMA and with the voluntary health agencies be encouraged.

Personnel of Workshop 4

Discussion Leader—Arthur Selzer, M.D., San Francisco, Chairman, Education Committee, Presbyterian Medical Center.

Secretary—Charles J. Tupper, M.D., Davis, Dean, University of California, Davis, School of Medicine.

Participants:

Ralph Bennett, M.D., Inglewood

Warren L. Bostick, M.D., Los Angeles, Dean, University of California, California College of Medicine

Donald Brayton, M.D., Los Angeles, Associate Dean for Postgraduate Medical Education, University of California, Los Angeles, Center for the Health Sciences

Fred L. Evans, M.D., Chico, Chairman, CMA Postgraduate Circuit Course—Chico

Thomas J. Fuson, M.D., Fresno, District Representative to the CMA Committee on Continuing Medical Education

L. S. Goerke, M.D., Los Angeles, Member, CMA Scientific Board; Dean, University of California, Los Angeles, School of Public Health

Ronald L. Kaye, M.D., Palo Alto, Chairman, Medical Education Council, Palo Alto Medical Clinic; Clinical Assistant Professor of Medicine, Stanford University School of Medicine

L. S. Donald Kimbrough, M.D., San Francisco, Chief Consultant on Communications, Continuing Education in the Health Sciences, University of California, San Francisco, Medical Center

Richard Lockwood, M.D., San Diego, Director of Hospitals and Clinics, University of California, San Diego, School of Medicine.

Mrs. Bettie Minifie, Los Angeles, Assistant Head, Continuing Medical Education, University of California, Los Angeles, Center for the Health Sciences

Glenn A. Pope, M.D., Sacramento, Member, CMA Scientific Board; Immediate Past President, California Society of Internal Medicine

Robert S. Quinn, M.D., Santa Rosa, District Representative to the CMA Committee on Continuing Medical Education

Glen Shepherd, M.D., Corona del Mar, Formerly Assistant Secretary for Continuing Medical Education, Council on Medical Education, AMA

W. Albert Sullivan, Jr., M.D., Minneapolis, Director, Continuing Medical Education, University of Minnesota School of Medicine; Member, Review Committee on Continuing Medical Education, AMA Council on Medical Education; Chairman, Committee on Continuing Education of the Association of American Medical Colleges

Raymond Tatro, M.D., San Bernardino, District Representative to the CMA Committee on Continuing Medical Education

David A. Wood, M.D., San Francisco, Chairman, Cancer Committee, CMA Scientific Board; Chairman, AMA Continuing Professional Education Committee on Voluntary Health Agencies; Director, Cancer Research Institute, and Professor of Pathology, University of California, San Francisco, School of Medicine.

Plan to Attend

CALIFORNIA MEDICAL ASSOCIATION

1968 ANNUAL SCIENTIFIC ASSEMBLY

*Fairmont and Mark Hopkins Hotels,
San Francisco, March 23-27*

EIGHTEEN SCIENTIFIC SECTION PROGRAMS ON A VARIETY OF
TOPICS PLUS FOUR GENERAL MEETINGS ON THE SUBJECTS:

- **THE MANY PROBLEMS OF BLOOD**
- **NEW DRUG THERAPY AND REACTIONS**
- **TRAUMA: PREVENTION, CAUSES, TREATMENT**
- **PSYCHEDELIC DRUGS**

THIRD CALL FOR

Scientific Papers

Medical Motion Pictures

Scientific Exhibits

★ **If you have a paper** you'd like to present to your colleagues during their section meeting . . . write today to your section secretary (names and addresses of scientific section officers may be found on page 6, Advertising Section of *California Medicine*). Presentations are not limited to the themes of the general meetings.

★ **If you have a motion picture or exhibit** . . . write to the California Medical Association Committee on Scientific Assemblies, 693 Sutter Street, San Francisco 94102, for application forms.

PLANS FOR THE 1968 ANNUAL SCIENTIFIC ASSEMBLY ARE NOW IN PROGRESS
PLAN **YOUR** CONTRIBUTION TO THE PROGRAM **TODAY**



WOMAN'S AUXILIARY

to the California Medical Association

WHAT IN RECENT YEARS in the Woman's Auxiliary to the California Medical Association has been called Community Service, now, according to the board of the Woman's Auxiliary to the American Medical Association, is to be changed to Community Health.

As the name is changed, so is the service program of your Woman's Auxiliary changed or added to when necessary to meet the needs of a constantly growing, expanding and learning medical world.

Health education is essential to national well-being and will be an integral factor in public and private health programs. Your Woman's Auxiliary has a service program that is designed to help with that education along with giving other services designed to help improve the health of your communities. It includes supplying health education materials (including venereal disease films, brochures and *Today's Health* magazine). Twenty county auxiliaries have active GEMS programs, nine last year participated in local Community Health Week programs; six reported Home and Traffic Safety programs; four regularly help staff their local blood banks. In connection with the stressing of youth health education, 13 counties have active programs on teenage venereal disease and juvenile delinquency. Nine counties have worked this past year with mental health and seven with programs of the aging.

Have you heard about your auxiliary's medical self-help courses? The courses are carried on under the Disaster Preparedness Program in the area, with the help of fire departments, physicians and nurses. Whereas first aid courses teach what to do

until a physician arrives, medical self-help is designed to teach what to do if a physician is completely unavailable.

There are no specific programs that your auxiliary is directed to carry out. Each area has its own problems, just as all age groups, childhood, youth, middle age and the elderly, have theirs. Materials are available on a variety of subjects; immunization, nutrition, help for handicapped, narcotics and drug addiction, alcoholism, venereal disease, smoking, prevention of heart disease, sex education, health aspects of aging, quackery, and many others. The Community Health Committee in each area selects the phase needed.

When a woman marries a doctor of medicine she automatically becomes a member of the Community Health Committee. From her wedding day on—consciously or unconsciously, with forethought or without it, effectively or ineffectively her membership on this committee is a reality. Her telephone conversations with patients, her contacts with friends and neighbors, and her service to the community as a physician's wife place her in that position. It is up to you physicians to help her become a very effective member of this committee by having her active in the Woman's Auxiliary to the California Medical Association, where she can become well informed on just how she can constructively help.

The success of the auxiliary is built on the ability of the group to change with the times—indeed they must be as up to date, on the medical needs of the world, as tomorrow.

MRS. JOSEPH L. PACE

Community Health Chairman

INFORMATION

Professional Courtesy

Adopted by Judicial Council of the American
Medical Association 17 June 1967

THE CUSTOM of professional courtesy embodies the ancient tradition of fraternalism among physicians in the art which they share, and their mutual concern to apply their learning for the benefit of one another as well as their patients. The Judicial Council reaffirms and endorses the principle of professional courtesy as a noble tradition that is adaptable to the changing scene of medical practice.

Professional courtesy is not a rule of conduct that is to be enforced under threat of penalty of any kind. It is the individual responsibility of the physician to determine for himself and within his own conscience to whom and the extent to which he shall allow a discount from his usual and customary fees for the professional services he renders, and to whom he shall render such services without charge as professional courtesy.

The following guidelines are offered as suggestions to aid physicians in resolving questions related to professional courtesy.

1. Where professional courtesy is offered by a physician but the recipient of services insists upon payment, the physician need not be embarrassed to accept a fee for his services.

2. Professional courtesy is a tradition that applies solely to the relationship that exists among physicians. If a physician or his dependents have insurance providing benefits for medical or surgical care, a physician who renders such service may accept the insurance benefits without violating the traditional ethical practice of physicians caring for the medical needs of colleagues and their dependents without charge.

3. In the situation where a physician is called upon to render services to other physicians or their immediate families with such frequency as to involve a significant proportion of his professional time, or in cases of long-term extended treatment, fees may be charged on an adjusted basis so as not to impose an unreasonable burden upon the physician rendering services.

4. Professional courtesy should always be extended without qualification to the physician in financial hardship, and members of his immediate family who are dependent upon him.



PUBLIC HEALTH REPORT

Lester Breslow, M.D., M.P.H.

Director, State Department of Public Health

THE U.S. SURGEON GENERAL expects substantial numbers of cases of influenza of the A2 type this season, particularly in the eastern sections of the country. He bases his prediction on the fact that Type A outbreaks usually occur every two to three years and type B every three to six years.

In California outbreaks of Type A are anticipated this coming season but not statewide. As a routine precaution, the Department of Public Health strongly recommends that persons of high risk be immunized against influenza. This group would include persons of all ages who have chronic debilitating diseases, particularly by those with rheumatic heart disease, cardiovascular disorders, bronchopulmonary diseases, diabetes mellitus and Addison's disease.

Patients residing in nursing homes, chronic disease hospitals and comparable environments should be considered at particular risk since their living arrangements may allow greater spread of disease once an outbreak begins. Some increased mortality was observed among pregnant women during the 1957-58 A2 epidemic, but not in subsequent years. Routine influenza immunization during pregnancy is not recommended unless the individual also is in one of the high risk categories.

Two influenza vaccine formulations are available for use in the 1967-68 season. A newly introduced bivalent vaccine contained only contemporary A2 and B strains is for general use to provide greater protection against current strains. The traditional polyvalent vaccine incorporates older strains (types A and A1) as well as new A2 and B antigens in order to stimulate a broader immunologic response. The older strains do not play a significant role against the currently prevalent viruses.

Both the bivalent and polyvalent vaccine formulations contain the same total quantity of influenza antigens—600 chick cell agglutinating (CCA) units. This limit is set in order to minimize the frequency of local and systemic reactions.

Persons who require immunization and have not

been vaccinated since July 1963 should receive a primary immunization series of bivalent vaccine. The primary series consists of an initial subcutaneous dose, followed by a second, two months later. Even a single dose can afford some protection.

Immunization should begin as soon as practicable after October 1 and ideally should be completed by early December. It is important that immunization be carried out before influenza occurs in the immediate area, because there is a two-week interval between vaccination and maximal development of antibodies.

Following is the recommended dosage:

- Adults and children ten years old and older, 1.0 ml subcutaneously on two occasions.
- Children six to ten years, 0.5 ml subcutaneously on two occasions.
- Children three months to six years, 0.1-0.2 ml of vaccine given subcutaneously on two occasions, separated by two to two weeks followed by a third dose of 0.1-0.2 about two months later.

Since febrile reactions in the younger age groups are common following vaccination, an antipyretic may be indicated.

Only a single booster of bivalent vaccine at the dosage level specified for the primary series is necessary for persons requiring immunization who have been vaccinated as recently as July 1963. This booster dose is best given in early December, before the beginning of the anticipated influenza season. For persons in older age groups who have previously had undue reactions to influenza vaccine, a booster dose of 0.1 ml given by intracutaneous injection can be expected to induce an antibody response somewhat comparable to that induced by the 1.0 ml subcutaneous dose. The intracutaneous route is not recommended, however, in other circumstances.

Since the vaccine viruses are propagated in eggs, the vaccine should not be administered to anyone who is hypersensitive to eggs or egg products.

NEWS & NOTES

NATIONAL • STATE • COUNTY

LOS ANGELES

Dr. Donald W. Petit, clinical professor of medicine at the USC School of Medicine, has been appointed program director of the **Regional Medical Program** grant awarded to USC, Dr. Roger O. Egeberg, dean, announced.

The regional program is part of a nation-wide project, financed by the federal government, to evaluate techniques for the distribution of optimum health care to patients with heart disease, cancer, stroke and related diseases.

* * *

Dr. Harry F. Dietrich, a private practitioner from Beverly Hills, has been selected to receive the American Academy of Pediatrics' 1967 **Outstanding Pediatric Practitioner Award**. The award will be presented to Dr. Dietrich during the Academy's annual meeting in Washington, D.C., October 21-26, for his outstanding services and contributions to the health and welfare of children. Dr. Dietrich has frequently addressed parent groups, and is an honorary life member in the California State Parent-Teachers Association. He has also lectured in the Los Angeles city school summer workshops for teachers and has extensively promoted the development of accident prevention programs.

* * *

The American College of Gastroenterology will hold its 32nd annual convention at the Biltmore Hotel in Los Angeles, October 29-November 1. Following the convention there will be a **three-day course in gastroenterology** at the Biltmore with a faculty selected from the medical schools in and around Los Angeles.

Further information may be obtained by writing to: Secretary, American College of Gastroenterology, 33 West 60th Street, New York, N.Y. 10023.

* * *

More than 800 **medical assistants** from throughout the nation will gather at the International Hotel in Los Angeles, October 11-15, for what

is expected to be the largest convention in the history of the 12,500-member American Association of Medical Assistants.

Highlighting this 11th annual meeting will be a series of symposiums showing AAMA members how they can prepare for roles of greater professional responsibility in meeting future medical needs. **Dr. Milford O. Rouse**, president of the American Medical Association, will be the featured speaker at a luncheon in his honor on the first day of the convention.

* * *

Clinical research **fellowships in oncology and cancer chemotherapy** are now available at the University of Southern California School of Medicine, under sponsorship of the National Cancer Institute. The fellowships are of one or two years' duration, and are available immediately, 1 January 1968 and 1 July 1968. Fellows will have broad patient responsibility and will supervise three residents. The Oncology Service comprises 60 beds plus an active outpatient clinic. Both standard and investigational chemotherapy is carried out under supervision of Dr. Jesse L. Steinfeld, chairman of the Western Cooperative Cancer Chemotherapy Group and professor of medicine. If desired, the fellowships can include a three-month rotation on the Hematology Service of Los Angeles County General Hospital. A year of fellowship can substitute for a year of residency for **board eligibility**. The stipend for the first year is \$6,000, of which \$3,600 is tax-free, and additional allowance is made for dependents.

Applicants should have completed one year of approved medical residency and be eligible for a California license. They should send a brief resume to Dr. David C. Stolinsky, USC School of Medicine, 2025 Zonal Avenue, Los Angeles 90033.

ORANGE

Dr. Edward Lee Russell retired as head of the Orange Health Department on 1 July. Dr. Russell began his service with the Orange County department in 1930 when he was appointed chief of the Division of Maternal and Child Health. He became the county's health officer in December 1939.

A pediatrician, Dr. Russell began his career in public health in Salem, Oregon, in 1928 with the Commonwealth Fund Child Health Demonstration. An outstanding feature of his career was

his ability to maintain a close relationship between the public health department and physicians in private practice in the community. In 1961 he was president of the Orange County Pediatric Society and he is senior attending physician and a trustee of Childrens Hospital of Orange County.

Dr. Russell continues as a valued member of the Editorial Board of CALIFORNIA MEDICINE.

SAN BERNARDINO

The American College of Physicians will sponsor a five-day **postgraduate course on clinical cardiology** in Loma Linda, October 2-6.

Dr. Varner J. Johns, Jr., professor and chairman of the Department of Medicine at Loma Linda, is course director. Associate director is Dr. Raymond B. Crawford, associate professor of medicine at the host university.

Faculty will be drawn from the university medical center, with guest lecturers from the National Heart Institute, Harvard University, McGill University in Montreal, Hahnemann Medical College and several medical centers in the Los Angeles area.

For registrations and applications, address: Dr. Edward C. Rosenow, Jr., executive director, American College of Physicians, 4200 Pine Street, Philadelphia 19104.

SAN FRANCISCO

The appointment of **Dr. Donald McKay** as professor of pathology and as chief of pathology service at San Francisco General Hospital was announced recently by Chancellor Willard C. Fleming and Dr. Stuart C. Cullen, dean of the School of Medicine at the University of California San Francisco Medical Center. Dr. McKay was formerly at Columbia University, where he was Delafield Professor and chairman of the Department of Pathology, College of Physicians and Surgeons. He is a native of Sacramento and is a graduate of the school he now joins as a professor.

SANTA CLARA

Two new appointments to the faculty of Stanford University School of Medicine have been

announced by Dr. Robert J. Glaser, vice-president for medical affairs and dean of the School of Medicine.

Dr. David Korn, a pathologist and senior investigator in the National Institutes of Health at Bethesda, has been appointed professor and executive head of the department of pathology, effective 1 June 1968.

The department of pathology has been without a permanent executive since Dr. Alvin J. Cox, Jr., professor of pathology, resigned in 1964 after 23 years of active leadership to devote time to research in dermatology.

Dr. Korn, whose interests lie beyond the field of pathology and extend into fundamental areas of biochemistry and mechanisms of life processes, is a senior staff member at the Laboratory of Biochemical Pharmacology of the National Institute of Arthritis and Metabolic Diseases, and an assistant pathologist at the National Institutes of Health.

Dr. F. Frank Zboralske has been appointed associate professor of radiology and head of the division of diagnostic roentgenology. He succeeds Dr. Herbert L. Abrams, who has been named professor and chairman of the department of diagnostic roentgenology at Harvard Medical School. Dr. Zboralske has been an assistant professor of radiology at the University of California Medical Center in San Francisco since 1965. At the medical center he also was director of the experimental radiology laboratory, chief of the section of gastrointestinal radiology and co-director of a research training grant in diagnostic radiology from the National Institutes of Health.

* * *

Dr. Richard C. Lillehei, professor of surgery, University of Minnesota Medical School, will deliver the fourth biennial **Albert M. Snell Memorial Lectures**, October 17 and 18, in the Palo Alto Senior High School auditorium, 50 Embarcadero Road, Palo Alto. The lectures are supported by the Albert M. Snell Memorial Fund, established in the Palo Alto Medical Research Foundation by Dr. Snell's friends and colleagues upon his death in 1960.

The Physician's BOOKSHELF



CALIFORNIA MEDICINE does not review all books sent to it by the publishers. A list of new books received is carried on page 49 of the Advertising Section.

DYNAMIC PSYCHIATRY IN SIMPLE TERMS—Third Edition—By Robert R. Mezer, M.D., formerly Instructor in Psychiatry, Harvard Medical School, and Assistant Professor of Psychiatry, Boston University School of Medicine. Foreword by Harry C. Solomon, M.D. Springer Publishing Company, Inc., 200 Park Ave., South, New York, N.Y. 10003, 1967. 182 pages, \$2.95 (paperback).

Dr. Mezer has succeeded in presenting current psychiatric concepts in a highly readable fashion. His writing is clear and understandable. He has necessarily had to compromise by oversimplifying his presentation of complex psychic processes. For example, in outlining the stages of psychosexual development, he follows the conventional abbreviated psychoanalytic model with relatively little attention to genetic, sociological and other factors that play important roles. The possible role of genetic factors in mental illness is not touched upon except for one reference to heredity in the discussion of manic depressive psychoses.

His definition of libido appears to be too broad and his indication that doctors in training to become psychiatrists routinely have a personal analysis is clearly an overstatement.

However, the book should continue to be useful to those who wish to get an overview of the principles of dynamic psychiatry. It should be helpful to students of medicine, nursing and other associated professions as well as to laymen who wish to obtain some understanding of the contemporary psychiatric approach to mental and emotional disorders.

NORMAN Q. BRILL, M.D.

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THE ART OF PREDICTIVE MEDICINE—The Early Detection of Deteriorative Trends (Proceedings of a Symposium)—Compiled and edited by Webster L. Marxer, M.D., Director, Diagnostic Survey Department, Beverly Hills Medical Clinic, Beverly Hills, California, and George R. Cowgill, Ph.D., Sc.D. (Hon.), Professor Emeritus of Nutrition, Yale University; Adjunct Professor of Biochemistry and Nutrition, University of Southern California, Los Angeles, California; Beverly Hills Medical Clinic, Beverly Hills, California. Program Committee, Wendell H. Griffith, Webster L. Marxer and Laurence E. Morehouse. Charles C Thomas, Publisher, Springfield, Illinois 62703, 1966. 358 pages, \$15.75.

This symposium was undertaken at the instance of a retail clerks' union and of its opposite number, an employers' group, with the aim, as stated on the jacket, "to examine the feasibility and advisability of launching a program aimed at the detection of deteriorative trends much earlier than has proved possible hitherto in periodic health examinations . . . for the purpose of preserving the individual's wholesome good health." The magnitude of the project is manifest in the size of the contributing groups, which consisted of 28 "participants" and 25 "observers" (who also joined in the discussions). The pro-

fessional competence of both groups appears to be high. Topics covered in detail are: Biology of aging, by Ralph V. Gerard; stresses in relation to disease, by Hans Selye; motivation, by Frank Fremont-Smith; the "style of life," by Lester Breslow; stress testing on aviation personnel, by Laurence E. Morehouse; performance evaluation and prediction, by Don Flickinger; biochemical individuality by Roger J. Williams; the laboratory in diagnosis, by Julius Sendroy, Jr.; human metabolism of amino acids and fats by Anthony A. Albanese; malnutrition, by Herbert Pollack; automatic instrumentation, by Wayland C. Griffith; data processing, by Richard Orr; demonstration cells, by Paul Weiss; deterioration in sub-cellular systems, by Lester Packer; some aspects of metabolic disease as bearing on early detection of deteriorative trends, by Laurence V. Kinsell; the state of the art of early detection of deteriorative trends in the cardiovascular system, by George C. Griffith; early detection of deteriorative trends in pulmonary function, by Ulrich C. Luft; serological screening tests for the early detection of chronic disease, especially cancer, by Charles M. Carpenter; future problems of virus infection, by Robert J. Huebner; the beginning of deterioration, by Nathan W. Shock; the cellular level of aging, by Leonard Hayflick; nutritional aspects of deterioration, by George J. Hamwi; and early asymptomatic diabetes (prediabetes), by Rafael A. Camerini-Davalos.

There is a summarizing discussion by Chairman Frank Fremont-Smith, with an addendum with concluding remarks by one of the organizers of the symposium, Webster L. Marxer.

This is probably not a volume for the general reader. It does afford a series of expert reviews of the different aspects of the aging process, while making it clear that a large amount of further research, including extensive use of computers, will be necessary before the age-old problem will be solved of finding a valid application of general principles to the specific needs of the individual which are so enormously varied. To quote the jacket again: "This concept of predictive medicine represents an attempt at a consideration of a continuing appraisal of the interesting dynamics of the Whole Man." The selection of the word "art" for the title instead of "science" seems apt.

H. K. FABER, M.D.

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MEDICINE AT THE PARIS HOSPITAL: 1794-1848—By Erwin H. Ackerknecht, M.D. The Johns Hopkins Press, Baltimore, Maryland 21218, 1967. 242 pages, \$8.95.

Professor Ackerknecht's *Medicine at the Paris Hospital 1794-1848* is an important book dealing with one of the most important periods in modern medicine. The first half of the nineteenth century saw not only the rise of

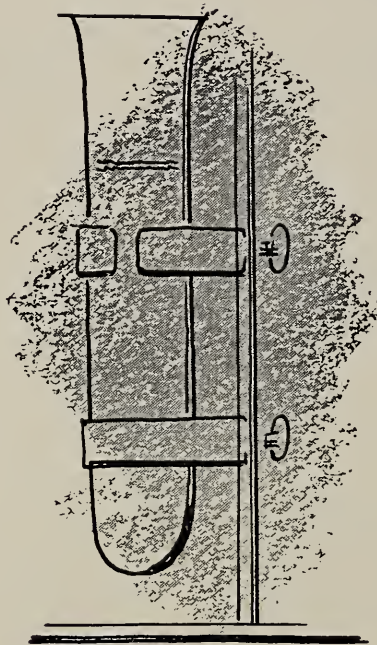
the Paris medical schools to a position of pre-eminence but gave new direction to the world of medicine based upon the then new techniques of physical examination,—of percussion, auscultation, thermometry, pathological anatomy, statistics—to establish clinical medicine of the form most familiar to the present day. Indeed, the names of the proponents of the new medicine are on the lips of clinicians almost every day.

In a series of brief but highly concentrated chapters, the author discusses the influence of the philosophy of the French Revolution in spawning the philosophy of the new medicine of observation and the extraordinary paradox by which the Revolution in seeking to abolish hospitals, medical schools and medicine secured the opposite by making the hospital the center of medicine, creating new vigorous schools and establishing a new era. Chapters are devoted to the major clinical figures Pinel, Bichat, Broussais, Corvisart, Bayle, Laennec; to the eclectics such as Andral, Magendie, Louis, Chomel, Rayer, Bouillaud; to the medical scientists, therapists, surgeons, hygienists and specialists; all of whom participated in perhaps the most creative period in the history of medicine and on the accumulated capital of whom we still draw in large measure. If the emphasis is on the clinicians rather than the medical and other scientists of the period, this has been done in order to highlight the nature of hospital medicine as such.

The book is short and highly concentrated. "In general,

I have tried to offer the essential elements of the story but to keep the book as short as possible. I wanted it to be read, not simply consulted as a kind of handbook." These aims are highly laudable. However, undue concentration often leads to ambiguity and error, as the absurdity (p. 193) of Sir William Osler inciting students from the United States to go to France in 1812, or the unsupported and unsupportable statement (p. 172) that Broca's speech center "was actually Gall's discovery." Above all, the brevity has been achieved by the sacrifice of style, so that the book, with the staccato sentence structure and recital of names, sometimes defeats its own aims by concealing the story in monotonous cadence. Despite these imperfections, it is an excellent work, sound in scholarship and of special significance to all physicians interested in following the forces which created modern clinical medicine. It is of special importance to California physicians, since the influence of French medicine was paramount in establishing its first institutions. The work is highlighted by Honoré Daumier's illustrations, originally prepared for the satirical poems of A. Fabre published in 1840. All in all, the reviewer can only agree with the author's own estimate of his work. "For several reasons, I like this book better than those I have written previously. I hope that, after perusing it, my readers will feel the same way." It is a "must" for the serious student of the development of medicine.

JOHN B. DEC. M. SAUNDERS, M.D.



Surgical Treatment of Mitral Insufficiency

JEROME HAROLD KAY, M.D., HAROLD K. TSUJI, M.D.,
JOHN V. REDINGTON, M.D., AND TARO YOKOYAMA, M.D., *Los Angeles*

■ *Sixty-four patients with pure mitral insufficiency were operated upon. Thirty of them had torn chordae tendineae. It was possible to repair the mitral valve in 57 patients and there were five operative deaths. One patient had a femoral artery embolus and another had a cerebral embolus. The incidence of peripheral embolization was 4 per cent compared with 40 per cent reported for ball valve replacement.*

Forty-eight of the 57 patients with repair (84 per cent) were living and well with at most a grade II/VI apical systolic murmur up to seven and a half years after operation. There has been no evidence of recurrence in these patients.

In approximately 90 per cent of patients with pure mitral insufficiency, repair should be performed. When feasible, repair is more satisfactory than valvular replacement, with not only excellent long-term results, but far less morbidity than is reported with ball valve replacement.

SINCE 1959 WE HAVE operated upon 64 patients with pure mitral insufficiency. All 64 patients had severe symptoms and were unable to perform their regular duties. The common complaints for these patients was pronounced fatigability on minimal exertions, orthopnea, inability to perform normal duties without dyspnea and paroxysmal nocturnal dyspnea. We have not operated upon any patients with mitral insufficiency no matter how large the heart nor how loud the murmur if the patient was asymptomatic. On the other hand we have not turned down any patient for operation because he was thought to be too ill. The 64 patients operated upon had normal or relatively normal valve tissue. However, in all cases the

mitral annulus was greatly dilated and in most cases the heart was very large. Thirty patients had torn chordae tendineae. This report consists of the results of operation on these 64 patients with pure mitral insufficiency unassociated with stenosis or calcification.

Results

Thirty-four of the patients operated upon had pure mitral insufficiency without torn chordae tendineae. In these patients there was gross annular dilatation, the mitral ring admitting four or five fingers (against two fingers normally). At the time of operation, using cardiopulmonary bypass, the valve was repaired in 30 patients. In four patients prosthetic valvular replacement was necessary. The technique of repair consists of placing sutures in the annulus of the mitral valve to narrow the valve to a two fingerbreadth opening

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Submitted 8 March 1967.

Reprint requests to: Cardiac Surgery, 1200 North State Street, Box 486, Los Angeles 90033 (Dr. Kay).

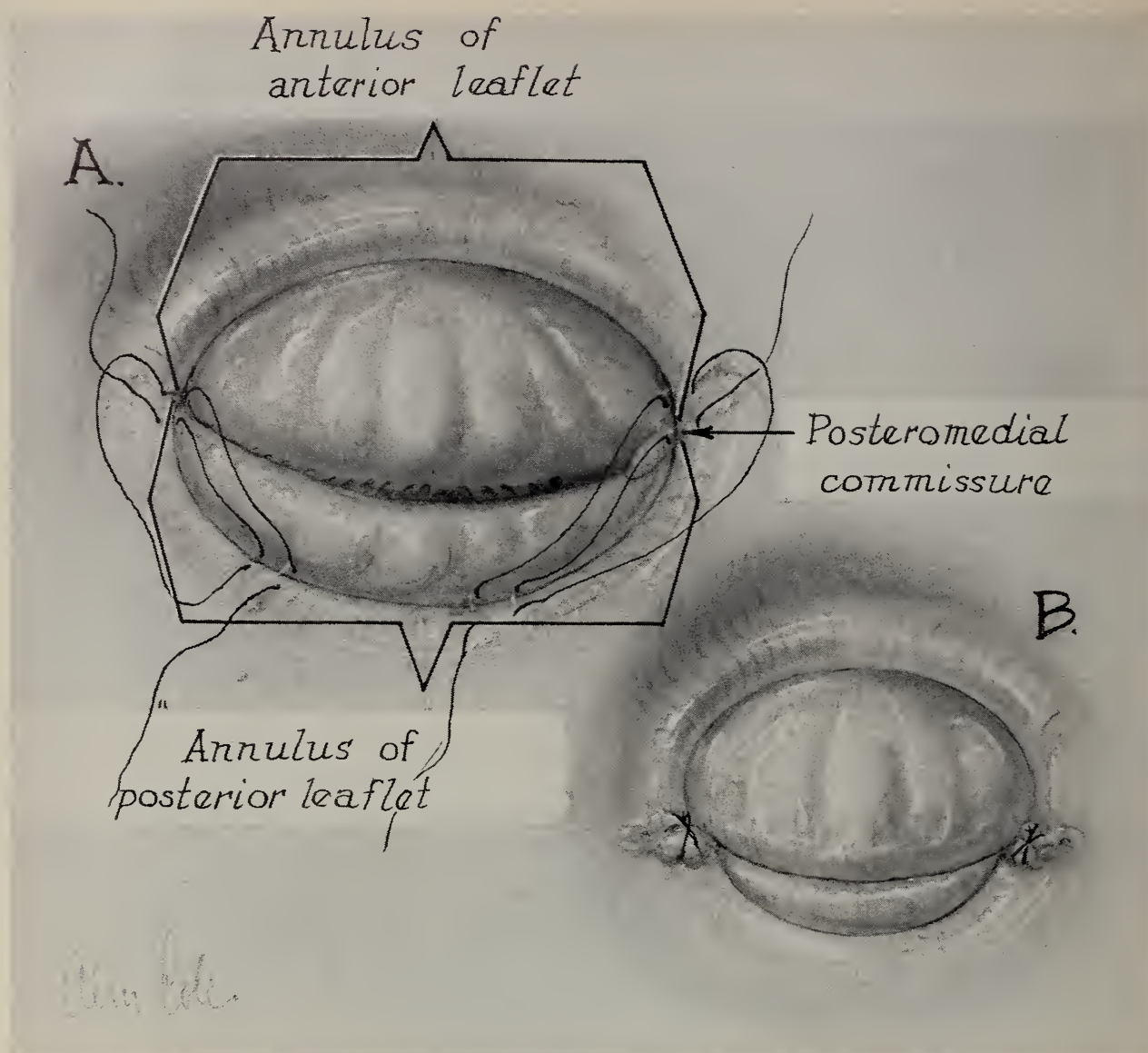


Figure 1.—Repair consists of placing sutures at the posteromedial annulus in such a fashion as to narrow the mural (posterior) annulus and preserve the aortic (anterior) annulus of mitral valve. In approximately one-fourth of the patients it is also necessary to place sutures at the area of the anterolateral commissure to accomplish competency.

(Figure 1). The sutures are placed in the posteromedial commissural area primarily and, in some patients, also at the area of the anterolateral commissure.

There were two operative deaths in the group of 30 patients in whom repair was performed. One death was due to renal shutdown and one death was in an extremely ill patient in pronounced failure. There were two late deaths. One late death occurred four months after operation and was due to serum hepatitis. The cause of the second death, which occurred five months after operation, is unknown as autopsy was not performed. In none of these patients was there evidence of peripheral embolization. The remaining 26 patients are alive and well six months to seven

and a half years after operation. These patients had a murmur of grade II/VI or less when last examined, and all were restored to a normal existence.

Thirty of the patients operated upon had torn chordae tendineae associated with annular dilatation. Most of the patients had four or five torn chordae which occurred on either the aortic (anterior) or the mural (posterior) leaflet and at any area along the valve leaflet. Infrequently there were two areas of rupture. It was unusual for these patients to give a history of previous bacterial endocarditis or myocardial infarction. The valve was repaired in 27 of the patients by sewing the involved portion of the leaflet down to the nearer papillary muscle and then narrowing the

annulus as previously described (Figure 2). There were three operative deaths. One death was due to postoperative bleeding and another was due to myocardial infarction due to encircling the circumflex artery with a suture. The third death was in a very ill patient with a large heart and in chronic failure.

There were two late deaths in this group of patients. The patients in both instances were in their fifties at the time of operation, and in both of them the mitral insufficiency was completely corrected. They survived three and four years, and postoperatively neither had a murmur. Autopsy examination in one of these patients revealed extensive coronary artery disease. Autopsy was not performed in the second patient, but he was thought to have coronary artery disease also. The remaining 22 patients have done extremely well and returned to normal activity with little if any murmur. A typical response of decrease in heart size in both groups of patients may be seen in Figure 3.

The youngest patient of the group of 57 who had mitral repair was two years of age and the

oldest was 66. Both of these patients did well and at last report had no murmur. In one of the 57 cases an embolus developed in the left common femoral artery within six weeks after operation. When last observed, six and a half years after operation, the patient had an excellent result and there was no evidence of further embolization. One other patient had a cerebral embolus eight days after operation, hemiplegia and aphasia resulting, but these conditions have somewhat improved since.

Discussion

Since 1959 when we adopted our present technique for the surgical treatment of mitral insufficiency, we have been pleased with repair of the mitral valve with pure mitral insufficiency.² The operative mortality in 57 patients with pure mitral insufficiency was 9 per cent. The embolic complications consisted of one cerebral embolus and one embolus to the common femoral artery. In 1959 and 1960 the patients did not receive anticoagulant therapy after operation. However, following

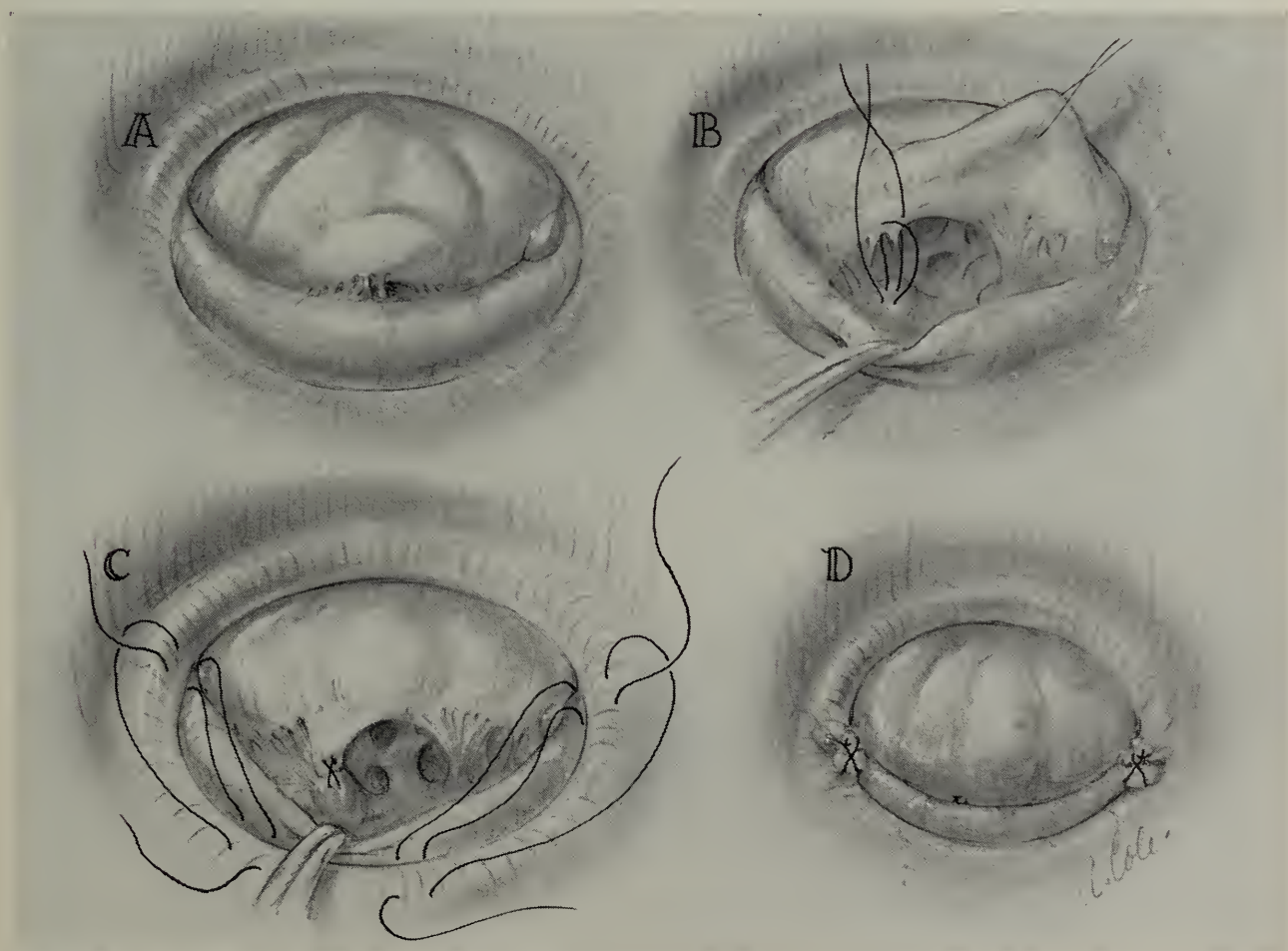


Figure 2.—Method of suturing the area of the valve leaflet with the torn chordae tendineae to the nearer papillary muscle. Following this the annulus is decreased in size.

the occurrence of the femoral artery embolus in one patient, all patients received coumadin therapy for four days after operation and were maintained on therapy with a prothrombin time around 20 per cent for three months, at which time the drug was discontinued.

In 1965, Herr, Starr, McCord and Wood¹ reported on special problems following valve replacement. They reported on 65 surviving patients with Starr-Edwards mitral ball valves who were observed for three months or longer. Twenty-six of them had at least temporary neurological deficit after cerebral embolization, and one patient died of a coronary embolus. Fifteen patients had residual neurological findings. In contrast, only one of our similar number of 57 patients in whom repair was carried out, had a cerebral embolus. Herr and coworkers¹ also reported on five fatal

cases of staphylococcal septicemia following mitral valve replacement. This complication was not seen in our patients with pure mitral insufficiency in whom mitral repair was performed.

It is important to note that in these patients with repair of the valve followed for six months to seven and a half years, there has been no evidence of recurrence of the mitral insufficiency. In fact in some patients a grade II/VI systolic murmur that was heard for the first year or two after surgery, disappeared in the ensuing years.

REFERENCES

1. Herr, R., Starr, A., McCord, C. W., and Wood, J. A.: Special problems following valve replacement, embolus, leak, infection, and red cell damage, *Ann. Thoracic Surg.*, 1:403-415, 1965.
2. Kay, J. H., Egerton, W. S., and Zubiato, P.: The surgical treatment of mitral insufficiency and combined mitral stenosis and insufficiency with use of the heart-lung machine, *Surgery*, 50:67, 1961.



Figure 3.—X-ray films before and six years after repair of mitral insufficiency.



Pinworms—

Incidence, Predictability and Treatment with Thiabendazole

JOHN A. KNOWLES, M.D., AND S. GEORGE EZEKIEL, M.D., *Oakland*

■ *One hundred-ninety-two children, ages 2 to 16 years, selected from the outpatient department medical clinic without regard to presenting complaint were examined by conventional cellulose tape specimens obtained at home. Twenty-four per cent of the patients were found to have pinworm ova present.*

The physicians seeing the last 84 patients were asked to estimate the likelihood of enterobiasis in these children. By various means from history, physical examination or blood cell differential counts, estimates were slightly better than by chance.

Treatment of 185 patients in a random fashion with placebo, thiabendazole and pyrvinium pamoate resulted in negative tests three weeks after therapy, in 15, 92 and 95 per cent of patients, respectively. Transient side effects consisting of anorexia and vomiting were noted in all three groups, but were most pronounced in adults receiving thiabendazole.

PINWORMS (genus of *nematode* of the family *Ascaridae* or *Oxyuridae*, genus *Enterobius*, species *E. vermicularis*) have been blamed as an etiologic agent for over 70 disorders from nymphomania to toxic synovitis.⁹ There is disagreement about many of these manifestations on a cause and effect basis; but there is no dispute that pinworms are the most prevalent helminthic infection in the United States and that millions of dollars have been spent in their eradication.

Interruption of transmission of this infection by vigorous hygienic and sanitary measures alone is extremely unreliable.¹⁴ "Cure" rates after treatment with piperazine citrate and pyrvinium pamo-

ate vary from 80 to 95 per cent, but recurrence is so frequent as to give many physicians reason not to treat at all. Piperazine must be given for seven days to be effective, while pyrvinium pamoate indelibly stains fabrics if it is spilled or vomited.

There is disagreement as to the causal role of pinworms in appendicitis, but most authorities agree that disagreeable confusing abdominal symptoms suggestive of this disorder may be a result of such infection.^{2,5} The incidence of pinworms in appendectomy specimens (0.6 to 13.0 per cent) may reflect geographic and socio-economic variables as well as method and diligence of the histopathological examination.^{1,13} During the past four years at this hospital, 29 (7 per cent) of 403 appendices removed at operation for appendicitis contained pinworms.

Children's Hospital Medical Center of Northern California, Oakland.

Submitted 8 February 1967.

Reprint requests to: Children's Hospital Medical Center Outpatient Department, Fifty-first and Grove Streets, Oakland 94609 (Dr. Knowles).

Purpose of Study

With estimates of infection of pinworms in urban areas of the United States ranging from 19 to 39 per cent of population,^{6,18} studied by multiple simple cellulose tape preparations,³ or by special swab methods, it was deemed important enough for us to establish our own clinic incidence by using a procedure that was compatible with that practiced in the offices of most physicians in the area. Second, we wished to determine if physicians in the outpatient department could predict if an individual patient was infected. And, if he could do better than by chance, what signs were reliable? Third, evaluation of a new broad spectrum antihelminthic drug, thiabendazole (Mintezole®), could be accomplished by treating cases found.

Method of Study

Two groups of patients were studied. In the first there were 181 children, ages 2 to 16 years, attending the general medical clinic. The subjects represented the first 181 children who: (a) Did not have a serious disease, and (b) were not being treated with antibiotics. The accompanying parent was given a small kit of slides, cellulose tape, mailing container and a sheet of printed instructions as follows:

Procedure for Preparation of Pinworm Slides

A. As soon as the patient awakens in the morning, before going to the bathroom, spread the buttocks so that the anus is exposed.

B. Take the piece of scotch tape given to you and with the sticky side toward the anus, press the tape securely to the perianal region.

C. Then stick the tape on to the exposed slides, with the sticky side attached to the slide.

D. Do this procedure on three consecutive mornings. After all three slides are completed, mail them in the postage-paid medical specimen box supplied to you.

One hundred and four kits were returned. The slides were examined either by one of the authors or by technicians in the hospital's clinical laboratory. If any one of the slides was found to be positive for ova, the patient was diagnosed as having pinworms. Twenty-seven of the 104 children had positive preparations (Table 1).

In the second part of the study, 151 children were similarly selected, but the physician seeing

TABLE 1.—Results of Screening

| | Positive | | Negative | |
|--------------------------|-------------|-------------|-------------|-------------|
| | Num- ber | Per Cent | Num- ber | Per Cent |
| First 104 Patients | 27 | 26 | 77 | 74 |
| Second 88 Patients | 19 | 22 | 69 | 78 |
| Total—192 Patients | 46 | 24 | 146 | 76 |

TABLE 2.—Predictability of Infection—Physicians' Estimates on Clinical Grounds, Compared with Diagnosis by Observation of Sticky Tape Pressed to Anus

| Physician's Estimate | Number of Patients | Positive by Testing |
|-------------------------|-----------------------|------------------------|
| Probably | 5 | 3 (60 Per Cent) |
| Maybe | 13 | 5 (39 Per Cent) |
| Unlikely | 66 | 11 (17 Per Cent) |

the patient was asked to judge the possibility of a pinworm infection. He was asked to estimate if infection was "probable," "maybe" or "unlikely."

Of the 88 kits returned, 19 were diagnosed as positive (Table 2).

All other family members of the 46 patients with positive tests were similarly screened for infection. In this manner a diagnosis of pinworms was made in an additional 72 persons. Each family was given a prescription to be filled at the hospital pharmacy. In a preselected randomized order the pharmacist filled the prescription with either a placebo, thiabendazole (Mintezole®), or pyriminium pamoate (Povan®), using the same agent for the whole family. The total dose of pyriminium pamoate was 5.0 mg per kg of body weight up to a maximum of 350.0 mg given as either tablets or suspension. The patients were instructed to take the entire amount as a single dose at supper time. Thiabendazole was given at 50 gm per kg per 24 hours divided into two doses per day for two days. Tablets or suspension were used. The placebo was given in form and dosage schedule comparable to that for thiabendazole. Medication was given to all family members even if the only positive test was in the first member tested. Approximately three weeks after taking the medication, repeat cellulose tape tests were done on all family members. The patients' cooperation in this follow-up was excellent. All but one family were rechecked (Table 3).

There were side effects noted in all three treated groups. These were inquired about at the three-week post treatment visit. At time of in-

TABLE 3.—Results of Treatment

| Treated With | No. of Family Members Tested | No. of Family Members Positive | No. of Persons Positive After Treatment | Per Cent | No. of Reactions |
|-------------------------|------------------------------|--------------------------------|-----------------------------------------|----------|------------------|
| Placebo | 60 | 41 | 35 | 85 | 2 |
| Thiabendazole | 65 | 37 | 3 | 8 | 14 |
| Pyrvinium Pamoate | 60 | 40 | 2 | 5 | 2 |

quiry the examiner did not know which medication the patient received. In one family of eight members treated with the placebo, two had abdominal pain that was thought to be related to the treatment. In one family of seven members treated with pyrvinium pamoate, one had diarrhea, another vomited twice. Fourteen persons in seven families (total 37 members) experienced a reaction attributable to the thiabendazole prescribed. This was chiefly nausea, vomiting and/or dizziness and occurred typically in the adults. The reaction in several patients was so pronounced with the first dose that the second dose was not taken.

Comments

Regardless of presenting complaint, 24 per cent of children seen in our outpatient department had laboratory diagnosable pinworm infection. In addition, when the families of infected patients were studied, 50 per cent of the remainder of the family was likewise infected. Rarely were the patients or the parents aware of their own infection.

Physicians who were specifically challenged to estimate the presence of pinworms in patients did a little better than could be expected by chance alone. It should be noted in this regard that an estimate of this kind is not all intuitiveness, as some reliance is put on a variety of clues—a history of previous infection, vague anorexia or equally nondescript abdominal pain, mild insomnia, perianal itching and physical findings of vaginal discharge, excoriations about the anus and low-grade eosinophilia on routine examination of blood. None of the parents at the time of this study described seeing pinworms.

Treatment with either thiabendazole or pyrvinium pamoate was extremely effective. Negative slides three weeks after therapy were obtained in 92 to 95 per cent of patients who previously had had slides positive for pinworms. Eighty-five per cent of patients who received placebos had positive slides three weeks post treatment. They did, however, serve as a control to test the reliability of the laboratory technique used to diagnose the infection. Late reinfection is a frequent occur-

rence despite the modality of treatment.^{7,16} We concur in the conclusion that pinworms need be treated only when symptomatic, and then with the simplest regimen available.

Reactions occurred with placebo, with thiabendazole and with pyrvinium pamoate therapy. The adults, especially in the thiabendazole-treated group, experienced the greater degree and frequency of side effects, usually dizziness, nausea and/or vomiting.

There are now two generally accepted medications for treatment of pinworms. Piperazine, used for many years, has few serious side effects except in children receiving unusually large doses,^{4,10} in those having abnormal electroencephalograms^{15,17} or idiosyncratic reactions.¹² Another disadvantage to piperazine is that, to be effective, it must be given over a seven-day period. Pyrvinium pamoate also has few side effects and needs to be given only as a single dose to be effective. It does occasionally, however, cause nausea and vomiting and is a strong dye, indelibly staining any porous material it comes into contact with, as it might by spilling or emesis. Thiabendazole has been observed to cause nausea and vomiting.^{7,8,11} It has the advantage of broad spectrum effectiveness with brief therapy and is not a dye. Its use will be limited in adults because of its side effects of dizziness, vomiting and anorexia. Clinical judgment is still necessary when selecting an antihelminthic for an individual patient.

Acknowledgments

The authors express their appreciation to William E. Worley, M.D., of Merck Sharp and Dohme Research Laboratories, West Point, Pennsylvania, for support of this study and for the thiabendazole (Mintezole®) used.

GENERIC AND TRADE NAMES OF DRUGS

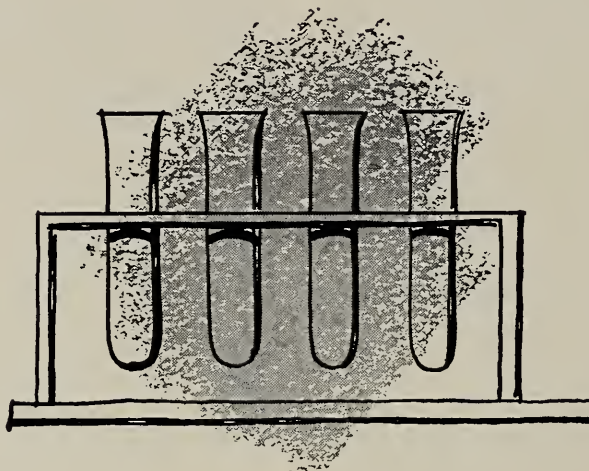
Thiabendazole—*Mintezole*.®

Pyrvinium pamoate—*Povan*.®

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Emergency Cardiopulmonary Resuscitation

A Fifteen-Month Experience in a General Hospital

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■ *Results under a resuscitation program in a general hospital in which the entire house staff is capable of functioning as a team in emergency, bear out the effectiveness of prompt action in cardiopulmonary or other life-threatening emergencies. Such a program remains important in spite of the salutary trend toward coronary care units. Both emergency and definitive therapy must be accomplished without delay. A house staff is necessary for an effective emergency resuscitation program. Paramedical personnel must be instructed to recognize an emergency and immediately institute life-sustaining therapy. Definitive therapy must be applied as soon as possible.*

The entire house staff, rather than a specially organized team, should be trained in the techniques of definitive therapy.

Consideration should be given to immediate defibrillation following diagnosis of cardiac arrest as an early step in definitive therapy.

NOW THAT EFFECTIVE resuscitation measures, particularly external cardiac massage and mouth-to-mouth breathing,^{2,4} are available for use in cardiac or respiratory arrest or other life-threatening emergency, the key to success in such emergencies is rapid mobilization of personnel and equipment.

Analysis of results of a resuscitation program that was established in June 1965 at Southern Pacific Memorial Hospital confirms the value of such a program and emphasizes the need for the entire house staff to be in readiness when the need arises. The hospital is a 350-bed general hospital, excluding pediatrics or obstetrics with patients ranging from 20 to 95 years of age. It has a house staff of approximately 40 residents and interns, with five house officers constantly on duty.

The system used in the hospital for quick mobilization of resources is as follows:

A case of cardiopulmonary arrest or other life-threatening emergency requiring immediate attention is signified through a coded message over the paging system announcing the location of the emergency. If a physician is not present at the site, emergency ventilation, and massage if needed, are carried out by paramedical personnel until additional help and equipment arrive. All house staff hearing the coded message respond, and the first physician who arrives takes charge of the personnel already on the scene and carrying out emergency measures. Simultaneously, a cardiac defibrillator and a cart equipped to handle most emergency situations are brought to the area. A designated group consisting of the physician of the involved patient and the medical and surgical residents on call, along with the cardiology resident and intern, is theoretically in charge of the re-

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Submitted 4 April 1967.

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TABLE 1.—Data on Resuscitation in Emergencies—84 Instances in 68 Patients

| Type of Emergency | Success | Failure | Temporary Success | Spontaneous Remission | Totals |
|----------------------------------------------------------|---------|---------|-------------------|-----------------------|--------|
| CARDIAC | | | | | |
| Ventricular fibrillation | 11 | 11 (2) | 2 | 2 | 26 |
| Ventricular tachycardia | 1 | 2 | 1 | | 4 |
| Cardiac asystole | 5 | 17 (2) | 1 | | 23 |
| Other arrhythmia | 4 | 1 | 1 | | 6 |
| RESPIRATORY | | | | | |
| Pulmonary emboli, asthma, infarct, hemorrhage, etc. | 3 | 8 (1) | | 2 | 13 |
| OTHERS | 6 | 4 | | 2 | 12 |
| Totals | 30 | 43 | 5 | 6 | 84 |

Legend: Survival greater than 1 hour=Success. Survival less than 1 hour=Temporary success. Inability to live without emergency support=Failure. Restoration without emergency support=Spontaneous. ()=Terminal case.

suscitation; but in their absence, or while awaiting their arrival, any other members of the house staff present carry out the definitive measures.

Results

Records were kept of all resuscitation attempts, excluding those in operating suites, between 1 June 1965 and 30 September 1966. There were 84 emergency attempts on 68 patients. Fifty-nine of the 84 were for cardiac arrest secondary to various arrhythmias, 13 for primary respiratory arrest, and 12 for various other causes, including six cases of acute hemorrhage (Table 1). Nine patients were discharged from the hospital (Table 2). Successful resuscitation, defined as a patient's survival without further emergency support for a period of more than one hour, was attained in 42 per cent of cases. More than 80 per cent of the patients who had artificial resuscitation had some measure of cardiovascular disease. There were 33 attempts on 26 patients who had acute myocardial infarction with subsequent complications.

Restoration of normal cardiac rhythm was accomplished in eight cases of ventricular fibrillation and two cases of asystole (Table 3). Excluding spontaneous remissions and terminal cases, there was a 12.5 per cent discharge rate (Table

4), slightly higher than the rates of 7 to 10 per cent reported elsewhere.⁶

Six patients were discharged from a group of 32 who were not "recent post-infarct" but had need for emergency attention (Table 5). Three of the six were among 13 patients with arteriosclerotic heart disease. The remaining three were from a miscellaneous group of patients with respiratory disease, trauma, convulsions and hemorrhage.

All patients were discharged without apparent neurological damage.

Discussion

The need for an emergency resuscitation program has recently been overshadowed by the advent of coronary care units for continual visual monitoring of patients with acute myocardial infarction. However, in our series, almost half of emergency calls requiring immediate medical attention did not involve post-infarction patients; over half of all emergency calls were on the wards or outpatient areas (Table 6.) There continues a need in a general hospital for an efficient and rapid emergency resuscitation program.

Any emergency resuscitation program is dependent upon swift and calm action on the part of medical and paramedical personnel. A successful program requires 24-hour coverage of the hospital by house officers, along with planning and training of both medical and paramedical personnel for various hospital emergencies, especially cardiopulmonary arrest.

Effective management of cardiopulmonary arrest can be divided into two parts: Emergency and definitive therapy.¹ Emergency therapy is the immediate life-sustaining application of external cardiac massage and mouth-to-mouth resuscitation. Paramedical personnel play a key role here, and

TABLE 2.—Number of Discharges and Type of Emergency—68 Patients

| Type of Emergency | Discharged Alive | Excluding Spontaneous Remission |
|--------------------------|-------------------------|---------------------------------|
| CARDIAC | 8 | 6 |
| RESPIRATORY | 1 | 1 |
| OTHERS | 3 | 2 |
| Totals | 12 | 9 |
| | 16.6 per cent survival* | |

*From 56 non-terminal patients, spontaneous remissions excluded.

TABLE 3.—Results of 32
Emergency Calls for
Post-Infarction Arrest

| Type of Arrhythmia | Success | Failure | Temporary Success | Spontaneous Remission | Totals |
|--------------------------------|---------|---------|----------------------|--------------------------|--------|
| Ventricular fibrillation | 8 | 4 | 4 | 2 | 18 |
| Ventricular tachycardia | | 2 | | | 2 |
| Asystole | 2 | 9 | | | 11 |
| Other | | | 1 | | 1 |
| Totals | 10 | 15 | 5 | 2 | 32 |

Legend: Survival greater than 1 hour=Success. Survival less than 1 hour=Temporary success. Inability to live without emergency support=Failure. Restoration without emergency support=Spontaneous. ()=Terminal case.

TABLE 4.—Number of Discharges and Type of Cardiac
Complication Following Myocardial Infarct

| Type of Arrhythmia | Discharged Alive | Excluding Spontaneous Remission |
|--------------------------------|---------------------|---------------------------------------|
| Ventricular fibrillation | 3 | 2 |
| Ventricular tachycardia | | |
| Asystole | 1 | 1 |
| Other | | |
| Totals | 4 | 3 |

12.5 per cent survival*

*From 24 patients excluding terminal and spontaneous remissions.

those intimately involved in situations which may lead to cardiac arrest should be trained in the cardinal points of establishing the airway, oxygenation and maintenance of circulation.

Definitive therapy is the attempt to correct the cause of the arrest. As has been well described elsewhere, this includes the differentiation between cardiac asystole or ventricular fibrillation, management of hypotension and acidosis, and correction of the offending arrhythmia, either with cardiotonic drugs, defibrillation or mechanical pacing of the heart.³ These diagnostic and therapeutic measures must be handled swiftly, since even the best emergency ventilation and circulation is marginal. Meanwhile, as body chemical relationships become more and more disarrayed, the chance for

successful restoration of normal cardiac action diminishes.⁵ The initiation of definitive therapy rests in the hands of the physician.

Hospitals with house training programs are in a particularly fortunate position in being able to effectively implement an emergency resuscitation program. A house staff is vital to such a program in order to provide the required constant medical coverage. All house physicians should be instructed and be conversant in definitive therapy, so that any group of physicians in the immediate vicinity of an emergency can proceed immediately with definitive therapy. This is of great advantage over the use of specially trained and "delegated" teams, for such groups would not (except fortui-

TABLE 5.—Number of Discharges and Kinds of
Emergencies in Patients without Recent
Myocardial Infarct

| Type of Emergency | Discharged Alive | Excluding Spontaneous Remission |
|--------------------------|---------------------|---------------------------------------|
| CARDIAC | | |
| Arteriosclerosis | 3 | 2 |
| Congestive Failure | 1 | 1 |
| RESPIRATORY | 1 | 1 |
| OTHERS | 3 | 2 |
| Totals | 8 | 6 |

16 per cent survival*

*From 32 non-terminal patients, spontaneous remissions excluded.

TABLE 6.—Data on
Emergency Calls Ex-
cluding Post-Infarction
Arrest

| Type of Emergency | Patients* | Emergency† Location | | | Success | Failure‡ | Spontaneous Remission |
|----------------------------------|-----------|------------------------|-----|------|---------|----------|--------------------------|
| | | Ward | ICU | OPD | | | |
| CARDIAC | | | | | | | |
| Arteriosclerosis | 8 | 2 | 5 | 2 | 6 | 3 | |
| CHF | 5 | 2 | 3 | | 1 | 4 | |
| RESPIRATORY | 12 | 6 | 6 | 1 | 3 | 8 | 2 |
| OTHERS | | | | | | | |
| Hemorrhage, trauma, etc. | 13 | 8 | 3 | 2 | 8 | 3 | 2 |
| Totals | 38 | 18 | 17 | 5 | 18 | 18 | 4 |

Legend: ICU=Intensive Care Unit. OPD=Other areas, X-ray, admitting office, etc. CHF=Congestive heart failure.

*Excluding terminal patients.

†Including repeat on same patient.

‡Excluding terminal second episode.

tously) utilize the nearest available physicians. Delay in instituting defibrillation, for example, may be fatal to a patient.

A review of our records shows that at any hour of the day at least three physicians arrived at the scene of an emergency within an average period of two minutes and often in less than one minute. Definitive therapy was immediately begun by the house staff. Such a response would have been impossible without house officers. We feel that this rapid response and immediate institution of definitive therapy has contributed to our results, which have been satisfyingly at or above the national average for such resuscitation programs. This has also provided the entire house staff with important training and experience in emergency resuscitation.

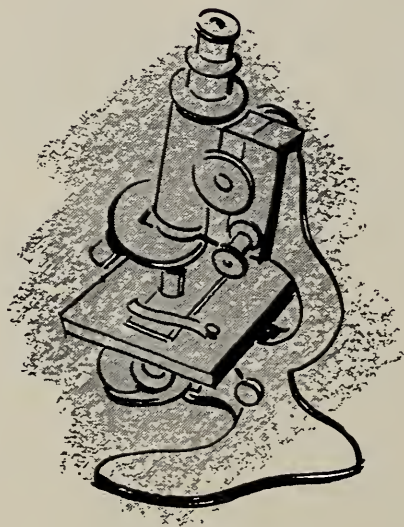
In our experience with cardiac arrest, the best results were in cases of ventricular fibrillation. However, acidosis resulting from even a brief period of cardiopulmonary arrest diminishes the effectiveness of the defibrillation, in spite of energetic emergency ventilation and cardiac massage. It has not been adequately emphasized that defibrillation upon detection of cardiac arrest by the clinician should be accomplished without undue delay. Perhaps too heavy reliance has been placed

on ancillary support and an attempt for definitive diagnosis via electrocardiography with the opportunity for defibrillation lost during the interim. Jude and coworkers² alluded to such a situation. Defibrillation should be emphasized as one of the earliest steps to be taken in definitive therapy. Certainly, considerable harm may result if it is delayed.

With proper application of emergency measures, more effective use of house physicians and earlier application of defibrillation, a resuscitation program may be even more successful.

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Appendectomy and Biopsy Despite Inflammatory Disease of the Bowel

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■ *For many years surgeons have preached against the removal of the appendix when regional enteritis is present. A high rate of fistulization and abscess formation supposedly follows appendectomy in such circumstances. This was not borne out in a series of cases in which appendectomy was carried out despite regional enteritis, granulomatous colitis and ulcerative colitis. Two fistulae occurred in 23 patients. Neither fistula was from the appendiceal stump.*

Appendectomy is probably a reasonable procedure when enteritis is present, although judgment should be exercised if there is appendicocolic involvement.

CONSIDERABLE CONTROVERSY exists over the advisability of removing any patient's appendix when regional enteritis affects that patient's small bowel or colon.

Because of the fear of impaired wound healing with fecal fistulization from the appendiceal stump, most surgeons are opposed to appendectomy in these circumstances. Residents are admonished never to perform such a procedure and wry smiles greet the surgeon whose patient has such a complication.

The distress of fistulization following so relatively simple a procedure is long remembered by both patient and physician; and the impression that this complication is ubiquitous has been supported by Colcock³ who reported a 25.6 per cent incidence of fistulization in such cases at the Lahey Clinic, and by Barber¹ who stated that the frequency of fistulization or abscess formation at

Mayo Clinic ran as high as 38.5 per cent after appendectomy.

In contradistinction, Crohn⁴ expressed the belief that appendectomy created no predisposition to the formation of fistulae; Ferguson⁵ discovered no fistulae secondary to appendectomy in cases he observed, and Marx⁶ found no evidence for fistulization from the appendiceal stump in a series he reported. Colcock³ believed that his position against appendectomy was well taken because the Lahey series demonstrated a 10 per cent incidence of spontaneous fistulization following laparotomy other than appendectomy, as compared with 26 per cent where appendectomy was performed. Crohn's⁴ statistics revealed the appearance of fistulization to be the same in the two situations.

Little differentiation is made in the literature between the results of appendectomy for acute regional enteritis and that performed incidentally on more chronic disease. Most of the investigators who have written on the subject imply that appendectomy in the face of the acute process is

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Submitted 10 April 1967.

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most fraught with danger, but Marx's⁶ report of a series of cases demonstrated that this may be less dangerous than supposed.⁶

The same problem holds for the extent of the disease. Most hospital records do not describe the extent and severity of the enteritis, especially with regard to colonic involvement. Even those investigators in favor of appendectomy balk at the procedure if the cecum seems to be heavily involved.^{5,6} And in all fairness to Colcock,² he said in his most recent article that appendectomy may be considered if the disease process is sufficiently distant from the ileocecal valve and cecum. Colcock³ and Barber¹ did not state the originating site of the fistulae in their earlier papers. Marx⁶ showed quite conclusively that the fistulae which had occurred in his series were not from the expected appendiceal site, but actually arose from the diseased ileum itself. Colcock² subsequently reported similar observations.

Certainly much of the confusion must relate to variables in the stage, extent, location and virulence of the enteritis; differences in dealing with the appendiceal stump; the use of steroids in pharmacologic doses; and the actual chronologic relationship between enteritis, appendectomy and fistulization. The statistics of such clinics as Lahey and Mayo may also be influenced by the fact that cases referred to them are more likely to be of complex nature.

Vigorous management of regional enteritis, granulomatous colitis and true ulcerative colitis at this institution (Stanford) has included parenteral steroids, salicylazosulfapyridine (Azulfidine®), local steroid enemas and construction of a double-barreled ileostomy proximal to the disease so that the defunctionalized distal bowel can be treated with both rest and local steroid instillations.

Ileostomy of this kind has afforded opportunity to electively remove the appendix in a number of cases despite enteritis. Further, where the exact diagnosis is somewhat in doubt, full thickness biopsy specimens of the bowel have been taken in areas of grossly active disease.

As it was believed that review of the complications attendant upon these procedures (appendectomy and biopsy) might shed some light on the problem, a study was made of all cases at this institution in which appendectomy was done in the face of enteritis or colitis—even cases in which the previously mentioned by-pass was not performed.

Materials and Methods

All cases at this institution in which appendectomy or bowel biopsy was carried out in patients who had acute or chronic regional enteritis, granulomatous colitis or ulcerative colitis were reviewed as to age, sex, diagnosis, duration of disease at the time of operation, follow-up, use of steroids, creation of ileostomy by-pass and fistula formation.

Data and Results

There were 23 such cases and the results of this review are tabulated in Table 1. There were four patients with granulomatous colitis, 12 with regional enteritis, and 7 patients with ulcerative colitis. Seven of the 12 patients with regional enteritis had clinical symptoms resembling those of acute appendicitis when first observed, and appendectomy was done despite the presumable taboo.

Sixteen patients had appendectomy only, one had bowel biopsy only and six had both. In two of these patients, fistulae developed during follow-up periods which varied from six months to nine years. Both patients had Crohn's disease and in both the fistulae originated not in the appendiceal stump but in the involved ileum. In one case fistula developed immediately after appendectomy (Case 13) and in the other a full year afterward (Case 11). Contrary to expectation, there were no fistulae following acute Crohn's disease and no fistulae in cases of ulcerative colitis.

In this small series the use of steroids did not seem to influence the occurrence of fistulization: In one case fistula developed in a patient receiving steroids (Case 11) and in the other case in one who was not (Case 13).

Discussion

Defunctionalization of the operative site may influence the development of fistulae and for this reason the present series may be weighted toward fewer complications of this type. In Case 11 the fistula developed before by-pass, following appendectomy at another institution. This factor is probably of particular importance where biopsy of the colon has been performed.

The observations in the present series agree substantially with Marx's⁶ findings that appendectomy can be performed where regional enteritis is present with reasonable assurance that the procedure will not materially increase the probability of fistulization beyond that of laparotomy alone. However, we can not be encouraged enough by this evidence to recommend appendectomy where

TABLE 1.—Clinical Data on 23 Patients in Whom Appendectomy or Biopsy Were Carried Out Despite Inflammatory Disease of the Bowel

| Case | Age and Sex | Disease* | Duration of Appendicitis (Years) | Operation* | Follow-up (Years) | Bypass | Steroids | Fistulization | Comment |
|------|-------------|----------|----------------------------------|------------|-------------------|--------|----------|---------------|--------------------------------|
| 1. | 76 F | UC | 5 | Ap Bx | 4 | No | No | No | |
| 2. | 30 F | UC | 20 | Ap | 3 | No | No | No | |
| 3. | 33 M | UC | 1½ | Ap | 2 | No | Yes | No | |
| 4. | 16 F | UC | ½ | Bx | 2½ | Yes | Yes | No | |
| 5. | 36 M | UC | 6 | Ap Bx | 2 | Yes | Yes | No | |
| 6. | 12 M | UC | 2 | Ap Bx | 2½ | Yes | Yes | No | |
| 7. | 19 F | UC | 2 | Ap Bx | 1½ | Yes | Yes | No | |
| 8. | 17 M | GC | 3 | Ap | ½ | Yes | Yes | No | |
| 9. | 49 F | GC | 4 | Ap Bx | 2½ | Yes | Yes | No | |
| 10. | 32 M | GC | 3 | Ap | 3½ | No | No | No | |
| 11. | 14 M | GC | 1 | Ap | 1 | No | Yes | Yes | Fistula from distal ileum only |
| 12. | 40 F | RE | 1½ | Ap Bx | 1½ | No | Yes | No | |
| 13. | 24 M | RE | ¼ | Ap | 1 | No | No | Yes | Fistula from distal ileum only |
| 14. | 26 M | RE | 1/3 | Ap | 1 | No | No | No | |
| 15. | 16 M | RE | 0 | Ap | 3 | No | No | No | Acute appendicitis when seen |
| 16. | 22 F | RE | 0 | Ap | 1 | No | No | No | Acute appendicitis when seen |
| 17. | 28 F | RE | 4 | Ap | 2 | No | No | No | Acute appendicitis when seen |
| 18. | 48 M | RE | 0 | Ap | 1 | No | No | No | Acute appendicitis when seen |
| 19. | 70 F | RE | 0 | Ap | 9 | No | No | No | Acute appendicitis when seen |
| 20. | 40 F | RE | 3 | Ap | 4 | No | No | No | |
| 21. | 48 F | RE | 0 | Ap | 6 | No | No | No | Acute appendicitis when seen |
| 22. | 25 F | RE | 0 | Ap | 1½ | No | No | No | Acute appendicitis when seen |
| 23. | 55 M | RE | 1/6 | Ap | 1½ | No | No | No | |

*GC=Granulomatous colitis; RE=Regional enteritis; UC=Ulcerative colitis; Ap=Appendectomy; Bx=Biopsy.

severe involvement of the cecum is apparent. Reasonable caution should still be exercised until further evidence pertaining to fistulization and severity of the local process is forthcoming.

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"Blind" Obturator By-Pass Graft Done with Tunneler and Obturator

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■ *A method for replacement of an arterial graft when sepsis develops in the groin involves "blind" passing of a prosthetic vessel from the pelvis via the obturator foramen to the popliteal space. This can be carried out with minimal dissection and no incision in the thigh. Adequate initial drainage, the use of antibiotics, locally and systemically, and suturing with monofilament polyester material appears to help toward a successful outcome.*

THE DISASTROUS results, both to limb and life, of sepsis in arterial grafting are well documented. Fortunately the incidence is low. Perhaps the most frequent site of infection is the groin with its superficial graft location, relatively "dirty" environs and lymphatic networks. Infection here can spell amputation or worse in aorto-femoral or femoral-popliteal procedures. Although the trend appears to be away from the use of prosthetic vessels below the inguinal ligament, certain problems will be encountered requiring prosthetic grafts from above or below to this area.

If such a prosthetic insert becomes infected, there are several alternatives for therapy, none of them entirely satisfactory. Graft removal with arterial ligation very likely will jeopardize the extremity. A trial of wide open drainage or local resection has been suggested and occasionally may be successful. Arterial autografts have also been used, but in my experience disruption and hemorrhage have resulted and I have abandoned this approach.

One hopeful aspect of the problem is that, with adequate drainage, infection with a patent graft appears to remain localized and not progress

along the graft tract. It would therefore appear that a method of completely by-passing the infected area might both preserve distal circulation and avoid continuing sepsis.

The use of the obturator canal to by-pass the infected groin has been reported.^{1,2,3,4} The methods described, however, involve the use of a medial thigh incision in rather close proximity to the groin wound, plus rather extensive dissection to pass the graft through this area. In order to avoid any thigh incision and dissection and thus avoid further sepsis, I have used a "blind" technique with a Cooley graft passer.* This instrument permits tunneling a graft with blunt dissection along the posterior-medial thigh to the popliteal space from the pelvis. The skin remains intact and the fascial planes are minimally disturbed. The advantages of such a method are obvious. It is suitable for both aorto-femoral or femoral-popliteal graft replacement when the groin is the infected site.

Method

The success of this technique lies in adequate initial open drainage of the groin. This would precede further manipulations by the time required for control of local sepsis and formation of clean

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*Manufactured by Robert Hoenig, Houston.

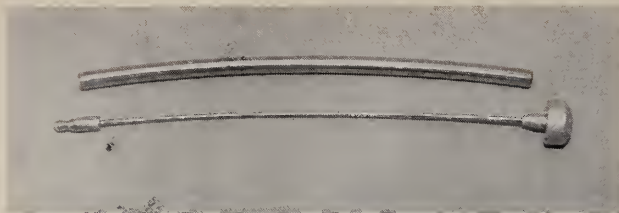


Figure 1.—Cooley graft tunneler with obturator.

granulating surfaces. With adequate local drainage and the use of monofilament polyethylene suture (Dermalene®) there is striking absence of continuing suture line infection and hemorrhage. This is contrary to my experience with the use of silk suture material. This plus a low incidence of suture failure and of false aneurysm has led me to abandon silk arterial suture material entirely.

Once local control is achieved, the groin is isolated by plastic drapes, the operation is begun with a transverse, transperitoneal or extraperitoneal abdominal incision and the proximal external iliac artery or prosthetic limb from aortic graft is exposed. Suitable anastomosis is then carried out and the obturator foramen is identified and its fascial membrane is incised medially. Medial incision avoids troublesome bleeding arising from



Figure 2.—Dacron Femoral-popliteal bypass with distal vein patch.

the vessels transmitted through the foramen laterally and anteriorly. The incision is dilated with the finger and then, with the patient's hip and knee somewhat flexed, a Cooley graft tunneler is introduced (Figure 1). It bluntly dissects easily along the posterior medial thigh and is then exposed at the popliteal space by the usual popliteal incision or by reopening the previous incision if the previous procedure was a femoral-popliteal by-pass.

If a previous graft is present it is cut off a few centimeters above the point of anastomosis to the popliteal artery and an end-to-end anastomosis is performed. The usual end-to-side anastomosis is done to the popliteal artery if this is a primary procedure. The old graft is then cut off high and, after copious local irrigation with an antibiotic solution, the graft stump is isolated from the popliteal space by tacking a portion of muscle over the graft tract.

The abdominal and popliteal wounds are then closed following antibiotic irrigations which supplement routine systemic administration of antibiotics. Graft removal at the groin with ligation of the common femoral, superficial femoral and profundus femoral arteries may follow in 24 to 36 hours to allow tract sealing. In aorto-femoral replacement procedures the lower anastomosis would be to the superficial femoral artery low in the thigh, or to the proximal popliteal artery. The distal graft segment is then removed through the groin, following isolation of the tract above with peritoneum or omentum. The groin incision is left

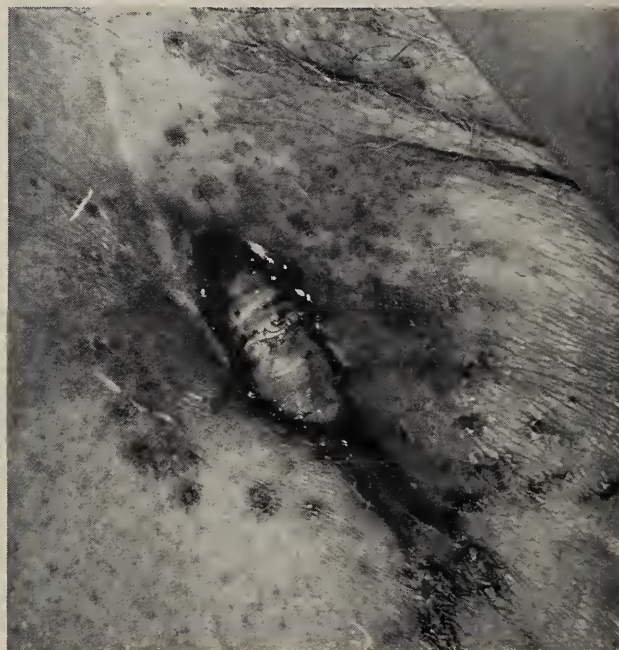


Figure 3.—Exposed infected graft in groin wound.

open and arterial ligation is carried out with monofilament polyethylene suture. Rapid healing follows.

Report of a Case

A 76-year-old woman with diabetes had two skin grafts to cover an indolent ulcer on the right shin in August 1964. Both grafts failed to heal and in November 1964 femoral arteriography revealed right superficial femoral thrombosis. Bilateral sympathectomy was done to promote healing and this likewise failed. In July 1965, right

femoral-popliteal by-pass with vein patch⁵ was carried out (Figure 2). (Suitable saphenous vein for vein bypass was not present.) The ulcer promptly healed, but a late infection of the groin wound with *Staphylococcus aureus* occurred. Open drainage and topical use of antibiotics stabilized the local infection, but healing did not follow these local measures (Figure 3). The graft remained patent and the wound granulated cleanly. In February 1966 an obturator by-pass graft, using the "blind" technique with an 8-mm dacron prosthetic vessel was done. Proximal anastomosis to the external iliac artery and a distal anastomosis end-to-end to the previous graft were carried out. No sepsis resulted and the groin wound rapidly closed following removal of the graft. A post-operative aortogram taken one month after the procedure showed good function of the graft (Figure 4). Six months after operation good pulses were present and ulcer healing was intact.

GENERIC TERMS

Polyethylene Monofilament (Dermalene®)—Manufactured by Davis & Geck, Danbury, Connecticut.

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Figure 4.—Functioning obturator by-pass, external iliac to popliteal artery, on right side.



Fitting of Temporary Prosthetic Limbs Immediately After Amputation

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■ *Better fit and function of prosthetic limbs is promoted when section and closure is done with attention to the prospective use of the stump as a pad for seating the limb. Preservation of tissue, fixing muscles to bone under physiologic tension, and making sure that bone ends are well covered with tissue are important to the comfort and usefulness of the limb that is to be fitted to the stump. Immediate application of a plaster-cast to form a total-contact socket for seating a temporary prosthetic limb, then early standing, weight-bearing and walking aid in healing and in shaping the stump to the permanent prosthetic socket it will ultimately occupy.*

RECENT DEVELOPMENTS in the care of patients requiring lower extremity amputations show great promise of improved results. These developments are the use of prosthetic-oriented amputation surgical procedures and the fitting of temporary post-surgical prosthetic limbs. These technical improvements have provided more effective and efficient amputee care than was our experience with standard techniques.

Standard Care

Although the problems of amputee fitting are significant in any age group, they are magnified in the geriatric population. At the Los Angeles County General Hospital⁶ between 1949 and 1959, prosthesis was prescribed in less than 10 per cent of 1,365 lower extremity amputations in patients over 55 years of age. And less than half of the patients in this group of presumably good candidates were consistent prosthetic users at the end of one year after they were fitted. Twenty per cent of the patients who had been fitted had

phantom pain. The great majority of amputees who were not fitted had become custodial problems to family or community. Two of the reasons which accounted for this dismal record were delay in fitting and the level of the amputation site.

In amputees of any age group, it is customary that there be three to twelve months' delay after amputation before the first prosthetic fitting. This delay is occasioned by the need to wait for stump maturity. Prosthetists are hesitant to fit a more recent amputee because early contour changes in the stump will require major and expensive socket modifications. Despite the delay, socket modifications are very frequently necessary within the first six months following prosthetic fitting, because of continued stump atrophy. In the case of the geriatric amputee, this delay is the breeding ground for progressive disability and weakness, joint contractures, deteriorating intellectual competence and social problems. As the elderly patient sits and waits, the mood of dependency quickly develops.

In more than 90 per cent of the amputations at Los Angeles County General Hospital in the 1949-1959 period, the level was above knee. Yet

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only between 20 and 50 per cent of the geriatric above-knee amputees can be expected to be effective prosthesis users.^{6,8} With the knee preserved, 70 per cent can be expected to be effective users.⁹

Historic Background

The first improvement in amputee care must be in the surgical procedure itself. In an earlier era, the accomplishment of patient survival and a healed wound were considered achievement enough by the surgeon, but today the operative risk is held to be so small that in training hospitals the most junior residents and interns are permitted to do amputations. From the standpoint of the surgical trainee, the success of an operation still must be graded by a healed wound and perhaps the speed of the job. As his training continues, the surgeon seldom comes face to face with the question of providing the kind of stump that can best be fitted with a prosthetic limb, for the business of fitting comes several months after the patient has left the hospital. So large was this void of surgical interest that an entirely new specialist, the physiatrist, emerged to supervise the fitting of a prosthesis.

There have been occasions when surgeons had to take an active concern in the problem of stump fitting. In post World War II Europe, the surgeons found no qualified prosthetists, certainly no physiatrists, but a great number of stumps. Faced with an amputee population of working age and a shortage of beds, the surgeons had to find some solution to the usual prolonged disability after amputation. In France and Poland, surgeons published the success of two technical changes to answer these needs.^{1,10} In an effort to achieve a stump that would not atrophy but would mature faster, the muscles were fixed to the end of a bone under physiologic tension. It was found that the functioning muscles in the stump provided a much improved feedback of spacial relations—that is, proprioception. The second technical change was in the provision of prosthetic function: The postoperative dressing was a total contact plaster socket to which a shank and foot were attached. The patients began standing on the amputated extremity within a few days and began walking in a few weeks. They usually walked out of the hospital on temporary prosthetic limbs by the first month. The advantages claimed for this technique over conventional methods are more rapid healing and maturity of the stump,

ability to return to work within two months, better proprioception in the stump and, most surprising of all, less than the expected amount of post-operative pain and very little phantom pain. After a presentation at the International Prosthetic Congress by Dr. M. Weiss of Poland in 1962, several American surgeons were encouraged to use similar techniques.

In the last four years, over 500 immediate post-surgical fittings have been accomplished under controlled circumstances at various medical centers. The group with the largest experience is Burgess and coworkers² of Seattle. In a consecutive series of 104 amputations, there was one wound infection and eight revisions to a higher level. Their ratio of below-knee to above-knee amputations was five to one. Most of the patients were in the older age group and had amputation secondary to vascular disease. The great majority of patients walked out of the hospital in less than a month. More than 80 per cent were functional prosthetic users when last observed.

Technique

Using essentially the same technique as that described by Burgess, we have had similar success. The principles of this technique are as follows: Especially in vascular cases, the amputation is performed with extreme respect for the soft tissue. Techniques developed by the hand and plastic surgeons are applied to the incision and the retraction of tissues. Speed is certainly not indicated. Muscles are not allowed to retract but are fixed to the bone under physiologic ten-



Figure 1.—Below-knee amputation stump ten days after operation, showing moulded contours at the distal end.



Figure 2.—Patient with a total-contact plastic socket on his left, two months after operation and a total-contact plaster socket on his right, one week after operation.

sion. The stump is shaped surgically to provide the most appropriate contours for the prosthesis (Figure 1). There can be no projections of skin or subcutaneous bone in the area of contact with the prosthetic socket, and the closed stump is neither flabby nor tense, but firm.

Following stump closure, the plaster total-contact socket is applied by the prosthetist while the patient is still asleep. Pressure areas are appropriately relieved and the plaster is moulded as necessary while it dries. The foot and shank are fixed at this time. For stability and suspension, the joint above the amputation is incorporated in the socket.

On the first postoperative day, the patient stands with partial weight on the stump. He progresses to parallel bars and then to a cane at his own rate. He is encouraged to be out of bed and as independent as possible. A total-contact plastic temporary prosthesis is fitted at two to four weeks (Figure 2). The patient walks with the temporary limb for many weeks until the stump gives no evidence of atrophy for at least a month. Once the permanent prosthesis is fitted, no major sock revisions are necessary.

Results

Over the last year and a half we have been involved with 44 immediate post-surgical fittings. Fourteen have been in private practice, 30 have been at Los Angeles County hospitals. Vascular disease was the cause of amputation in 36 of the patients, the oldest of whom was 78. No above-knee amputations were done in the vascular disease patients; four had revisions to higher below-knee or to through-knee levels. There was one wound infection, secondary to fecal contamination after a postoperative enema. All patients, using temporary prosthetic limbs, were ambulating in parallel bars by the first week.

All patients who worked went back to their jobs—the earliest four weeks and the latest four months after operation. All private patients ambulated without a support and were discharged from the hospital within five weeks after operation, most of them within three weeks.

In the case of the county hospital patients, all became ambulatory. Ten needed assistive equipment such as walkers or crutches. All were eventually discharged from county hospitals to their families or to board and care facilities as capable of self-care. The earliest discharge was four weeks and the latest six months after operation. None of the patients has had persistent phantom pain. None is receiving analgesic drugs for pain referable to the amputation.

Discussion

Experience with this technique has led us to several changes in concept. The use of a temporary total contact prosthesis is a more effective measure to mature a stump than traditional elastic bandage wrapping. The physiologic pumping action of gait provides a force more effective than a bandage. This point was confirmed by our experience at the Los Angeles County Hospital Prosthetic Clinic. Amputations at this clinic had been done by standard techniques. All patients are now placed in a total-contact plastic temporary prosthesis as soon as they are seen. Stump wrapping is discouraged. Stump maturity is consistently achieved in less than two months if the patient uses the temporary prosthetic limb. Frequently the patient is one who has been unable to obtain a mature stump by a previous attempt at stump wrapping for four to six months.

Another surprising observation is that the wound can heal well under the apparently adverse

conditions of weight-bearing. In fact, it has been our experience that, when the blood supply is good, the wounds appear to heal faster than expected. In support of this observation, there is considerable experimental evidence that connective tissue heals most efficiently when the environmental stress of function is applied early in the healing stage.^{3,4,7} In cases of deficient blood supply at the wound edge and minor wound separation at the line of the first change of cast, continued ambulation does not cause a further deterioration of the wound. Continued ambulation with the temporary prosthesis results in eventual healing.

Probably the most significant development associated with this technique is the focus of attention upon the stump as a functional extremity. The surgeon now extends his interest past the problem of patient survival and wound healing to the problem of building the most serviceable tissue possible. The prosthetist for the first time has the opportunity to mold the stump to its most functional dimensions while the tissues are in their plastic healing stage. The separate points of view of the surgeon and the prosthetist are forced to meet over the healing stump. Both must take

responsibility for the eventual success or failure of the patient as a prosthesis wearer.

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Legalized Abortion in Japan

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■ *The enactment of the Eugenic Protection Act in Japan was followed by many changes. The population explosion was stemmed, the birth rate was halved, and while the marriage rate remained steady the divorce rate declined. The annual total of abortions increased until 1955 and then slowly declined. The highest incidence of abortions in families is in the 30 to 34 age group when there are four children in the family. As elsewhere abortion in advanced stages of pregnancy is associated with high morbidity and mortality.*

There is little consensus as to the number of criminal abortions. Reasons for criminal abortions can be found in the legal restrictions concerning abortion: Licensing of the abortionist, certification of hospitals, taxation of operations and the requirement that abortion be reported. Other factors are price competition and the patient's desire for secrecy.

Contraception is relatively ineffective as a birth control method in Japan. Oral contraceptives are not yet government approved. In 1958 alone 1.1 per cent of married women were sterilized and the incidence of sterilization was increasing.

AT THE END OF WORLD WAR II Japan had several pressing reasons for legalizing abortion. The repatriation of Japanese citizens from territory lost in the war accentuated the crowded conditions in an already densely populated land. The marriage and birth rates were at record highs.² The postwar depression placed heavy demands on health and welfare departments.

Moral and religious opposition to abortion was not strong. Infanticide had been practiced in Japan for several centuries, and by comparison abortion was a more humane solution to the population problem. The Catholic Church probably represented less than 1 per cent of the people and followers of the Shinto and Buddhist religions did not object to a significant degree.

On 13 July 1948 the Japanese Diet passed the

Eugenic Protection Law which broadened the indications for abortion and sterilization to the extent that anyone could legally obtain them. Abortion was limited to the removal of non-viable contents of the uterus and sterilization was to be performed without removing the gonads or the uterus and without using x-rays.⁵

The subsequent passage of the Medical Service Act provided for periodic inspection of, and reports from, hospitals approved for abortions and sterilizations. Special licenses for performing abortions and sterilizations were issued by the medical societies of the 46 prefectures. In urban areas licenses were usually limited to specialists in obstetrics and/or gynecology. By 1951 the special licenses had been issued to 8,000 of Japan's 84,000 physicians.⁵ Contraception has had a slow start in Japan and today lags far behind abortion as an effective birth control method.⁶

Submitted 31 October 1966.
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Vital Statistics Following the Eugenic Protection Law

In the first eight years the birth rate per 1,000 population fell from 34.3 to 17 and has remained at this low level up to the present.² This rate exceeds the death rate by two and a half times,² but because the average age of the population is low the death rate is expected to rise so that by 1995 it should equal a slightly further lowered birth rate.⁴ The present population of about 100 million is expected to reach a peak of 113 million in 1995 and then slowly decrease.⁴

The marriage rate per 1,000 population reached a peak of 12 in the first postwar year (1947), dropped to eight in 1951, and since then has gradually increased to the present level of 10.²

The divorce rate per 1,000 population stayed close to 1.0 between 1947 and 1956, when it began falling to the figure of 0.73 in 1963.²

The maternal death rate per 10,000 live births remained at 16 from 1947 to 1956, when it began declining to the 1963 figure of 9.3.²

Between 1947 and 1963 the neonatal death rate per 1,000 live births fell from 31.0 to 13.8.²

The stillbirth rate paralleled the rise and fall of reported abortions.^{2,4}

Number of Reported Abortions

The number of reported abortions reached a peak of 1,200,000 in 1955 and slowly declined to 985,000 in 1962, the date of the last available report.⁴ A downward trend appears also in surveys of 1953-1954 and 1958. In the Yokohama area survey of 1953-1954 it was found that the ratio of abortions to live births was 1:15.³ In the 1958 survey in Shizouka prefecture it was found that the ratio had dropped to 1:2.4.⁷ The wide discrepancy in these figures is partly explained by the 15 per cent fall in the birth rate during this interval.²

Whether the abortion rate is actually falling is open to question. Between 1957 and 1959 it has been estimated that for every birth prevented by contraception there were 2.5 births prevented by abortion.⁶ Furthermore it appears unlikely that the present reporting of abortions is as conscientious as in the years immediately following the passage of the Eugenic Protection Law.

Abortion in Relation to Family Size And Marital Status

Surveys by the Institute of Public Health of Tokyo in 1950 and 1961 show a radical change of attitude about large families. In 1950, 29.8 per cent of mothers with two children said they

wanted no more. Eleven years later this figure had risen to 64.2.⁶

The Shizouka prefecture survey of 1958 showed that the highest incidence of induced abortions in married women occurred in families of three or four children.⁷ The frequency of abortion in unmarried women can be guessed at by comparing figures of this survey with an 18-month record at the Sumida Hospital in 1953-1954.⁷

| Number of Children | 0 | 1 | 2 | 3 | 4 | 5 | 6 | Total |
|--------------------|-----|-----|-----|-----|-----|-----|-----|-------|
| *Shizouka | 1.3 | 4.1 | 4.7 | 6.1 | 6.3 | 4.8 | 4.0 | 4.6 |
| †Sumida.. | 365 | 369 | 555 | 523 | 366 | 149 | 88 | 2,415 |

Abortion in Relation to Age

In the Shizouka survey the number of induced abortions in married women was divided into five-year age groups.⁷

| Age Group (Years) | 15-19 | 20-24 | 25-29 | 30-34 | 35-39 | 40-44 | 45-49 |
|---------------------|-------|-------|-------|-------|-------|-------|-------|
| Number of abortions | 2 | 63 | 320 | 342 | 262 | 123 | 15 |

Cost

The cost of early abortion is usually below \$15. However, foreigners have reported paying as high as \$125. Many industries pay for abortions for their employees as a fringe benefit and as protection against high turnover of labor.

Techniques of Abortion

Pommerenke⁵ reported visiting six hospitals in which abortions were being performed in 1954 and described techniques which were generally inferior to American standards. In any of the hospitals surgical gloves were not used. Until the fourth month of pregnancy the usual method was dilatation and curettage. Also used were plastic intrauterine devices, quinine, ergot, styptics of iron iodine and silver salts, as well as thermocautery and thermocoagulation (after the heat of the instruments was routinely tested on raw beef just before use). In the fourth month gauze wicks, vaginal packing, dried plant stalks, seaweed, rubber bougies, metallic cannulas and cervical incision were used. After the fourth month irrigation with a stannous solution and the Abural method (suprapubic intrauterine injection of saline solution) were used.

*Number of induced abortions per 100 family women capable of pregnancy.

†Total induced abortions in married and unmarried women.

Complications

Questionnaire data concerning 21,936 induced abortions in 1951⁵ were studied. In 143 of the 184 seriously complicated cases (which included 10 deaths) the method was dilatation and curettage; in 15 bougies were used, in 16 the Abural method, and in 10 hydrostatic bags. In only 130 of these 184 cases was the abortion performed by a licensed physician.⁵ Thus it appears that unqualified personnel and advanced pregnancy were significant factors in the complicated cases.

Illegal Abortions

In Japan, as elsewhere, a close estimate of the number of illegal abortions is impossible. Apparently many illegal abortions are performed in physicians' offices under fairly good conditions. Among reasons for clandestine abortions are the physician's desire to avoid taxation (each operation is taxed) and the patient's desire for secrecy or for avoiding the expense of a mortician (which is required when an advanced pregnancy is aborted).

Contraception

The government first condoned the use of certain contraceptives in 1951 and in the following year appropriated a small amount of money for the dissemination of contraceptive information. A survey by the Ministry of Welfare in 1954 disclosed that only 36 per cent of fertile women had ever used contraceptives or practiced contraception. In 1959 the condom was the most popular, and then, in order, the rhythm method, pessaries and spermicides.¹ In the same year 58 per cent of reported abortions were performed because of failures of contraceptive methods.

For several reasons optimal application of contraception has not been achieved in Japan. Although physicians and midwives (midwives deliver about 95 per cent of Japanese babies) are asked to promote contraception, midwives are not allowed to dispense contraceptives. Because abortion is often paid for by social insurance or the employer, it is cheaper than contraception. Oral contraceptives have not yet been approved by the government.

The Institute of Public Health in Tokyo provides annual courses of three to four weeks on marriage counselling and contraception.

Sterilization

The Eugenic Protection Law permits voluntary sterilization and authorizes a special council to force sterilization under certain conditions. The reporting of sterilizations is requested but not obligatory; therefore the reported figures must be lower than the actual.

Vasectomy and cornual cauterization were the methods commonly employed in the 1950s. Yasuis (cited by Pommerenke) using cornual cauterization, reported a subsequent pregnancy rate of 4.4 per cent within three months in 299 cases in 1951.⁵ Since then the popularity, and presumably the dependability, of sterilization has greatly increased.⁵

In 1951 the recorded sterilizations were one per 40,000 population, the female:male ratio being 60:1.⁵ The Shizouka prefecture survey of 1958 showed that 3 per cent of women of child-bearing age had been sterilized and that the female:male ratio was 31:1.⁷ That sterilization was still increasing at that time is suggested by the fact that one third of this 3 per cent had been sterilized in the year 1958 alone. The highest incidence of sterilization was in the 30 to 34 age bracket among women who had had four children. The Shizouka survey also showed that the rate of sterilization was four times higher in women who had had two or more abortions than in those who had had only one abortion.

Sterilization costs two to three times more than an abortion,⁵ and unless ordered by the Eugenic Protection Council must be paid for by the patient. It is understood that if a sterilization operation fails to prevent pregnancy it will be repeated free of charge.

Addendum

The total number of reported induced abortions continued to decline in 1963 and 1964. The figures were, respectively, 955,092 and 878,748.

As of March 1967, the Japanese government had not yet approved the use of oral contraceptives.

Source: Muramatsu, Minora: Japan's Experience in Family Planning—Past and Present, Family Planning Federation of Japan, Inc., March 1967.

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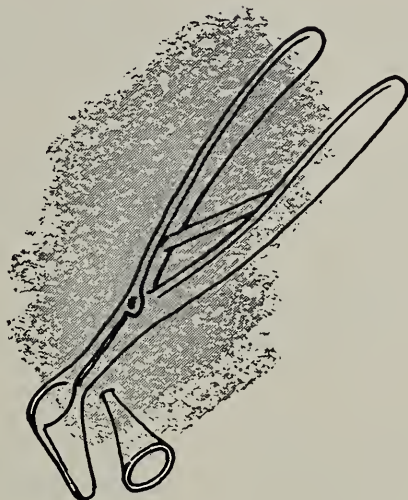
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Biology of Human Trophoblast

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THE PLACENTA IS AN organ which occupies the intermediate zone between the maternal and fetal organisms. As such it may be an active or inactive participant in the effects each organism has on the other. In some cases it may independently initiate activity by virtue of its synthesis of biologically potent substances.

The principal cellular component of the placenta at term is the syncytial trophoblast. This cell is an epithelial tissue lining the placental maze more or less completely; as such it is interposed between the maternal and fetal blood systems and probably is the major tissue responsible for whatever properties are assigned to the placenta. From observations in recent years, knowledge of functions of the syncytiotrophoblast has considerably increased and this cell has been shown to possess extraordinary abilities.

This review is concerned particularly with the biology of the human placental trophoblast. This tissue's role in the transport of substances, the production of hormones and its propensity for migration as well as certain immunologic characteristics will be discussed.

Histology

The human placenta can be likened to a forest of weeping willows with the roots in the fetal side and the trunks directed toward the maternal side, with numerous branches called chorionic villi. The chorionic villi, containing networks of capillaries which are directly continuous with the umbilical vessels, are bathed in a lake of maternal blood. Lining the chorionic villi as well as the peripheral limits of this intervillous space is this peculiar tis-

sue called trophoblast. It has certain electron microscopic features usually associated with epithelial tissue.²⁸ We will be concerned primarily with that trophoblast which lines the branching chorionic villi.

Like the placenta as a whole, the trophoblast derives from fetal tissues, and, in humans, it is made up of two layers of cells. The outer layer which is the lining tissue and in direct contact with the maternal blood is multinucleated and continuous. No cell boundaries have been identified within it.²⁸ Its cytoplasm, which stains well, ultra-microscopically is loaded with complex organelles usually associated with manufacturing capabilities. This cell is considered to be well differentiated. The inner or Langhans layer, quite prominent during the initial three months of pregnancy, is composed of mononucleated cells which are considered undifferentiated.²⁶ Their cytoplasm stains poorly and has sparse content of submicroscopic particles (implying a limited function). These cells are called cytotrophoblasts and are present throughout pregnancy, although in substantially diminished numbers toward term.³⁸

The relationship between these two layers of the trophoblast has been a perennial question. It had been noted that mitoses were seen in cytotrophoblasts but never in the multinucleated trophoblast. Recent calculations of the desoxyribonucleic acid content of the multinucleated trophoblast's nuclei confirmed the inactivity of these nuclei with respect to division.¹¹ Subsequently, by using techniques wherein radioactive thymidine was incorporated into recently divided nuclei to permit microscopic recognition, it was demonstrated both in human placental tissue in culture and in pregnant rhesus monkeys that cytotrophoblastic nuclei were labelled initially; and

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only after an elapse of time was the label noticed in the multinucleated layer.^{22,34} Even then the nuclei in this layer nearest to the cytotrophoblast were labelled first. Concurrent studies employing electron microscopy were able to identify cells which appeared to be of an intermediate type between the mono- and multinucleated varieties. This intermediate cell was mononucleated and possessed a cytoplasm which contained submicroscopic organelles. Recognized in the multinucleated trophoblast were bits of cell membrane which were interpreted as representing the remains of the cytotrophoblast cell membrane.²⁷ These findings have led to the current view that the multinucleated trophoblast is derived from an amalgamation of the cytotrophoblastic cells which serve principally as precursor cells. Being a product of a fusion of cells, this multinucleated layer is referred to as a syncytium or syncytial trophoblast.

Transfer of Substances

At one time considered to be the principal function of a placenta, acting as the clearing station for substances between the fetal and maternal organisms still must be considered a prime placental responsibility. However, no longer can the placenta's role be considered merely that of a semipermeable membrane.

Recent studies have shown that various substances may exist in different concentrations in the maternal and fetal blood streams. Amino acids, water-soluble vitamins, inorganic phosphate and fructose are found in higher concentrations in the fetal blood. Fat-soluble vitamins are found in higher concentrations in the maternal blood. Various mechanisms have been implicated to account for these gradients, and the responsibility for the success of these mechanisms is usually ascribed to the placental trophoblast. The mechanisms include simple diffusion, active enzymatic transfer and pinocytosis.²⁵ Active enzymatic transfer and pinocytosis require energy and complicated intracellular prerequisites. Ultramicroscopic studies are beginning to supply evidence concerning the syncytial trophoblast's qualifications in this regard.

Microvilli, pinocytotic vesicles and decidedly convoluted basal membranes, considered to be ultrastructural modifications of cells involved in active transport of water and electrolytes, are found in the multinucleated syncytial tissues.^{1,28,39} Furthermore, series of narrow canals and vesicles

traverse the entire thickness of syncytiotrophoblast between the maternal blood stream and its basement membrane. Since it was unclear whether these canals were continuous, it was proposed that they might be likened to a canal system with locks. Substances can apparently cross the syncytial trophoblast contained within these canals without being exposed to the cytoplasm. At the same time microvilli and "pits" were found in these transcellular canals and were believed to provide sites at which modifications of en route substances could take place.¹ Among modifications that it was suggested might occur here were the degradation and absorption of certain proteins providing a source of peptides to the fetus, and the structural alteration of complex carrier molecules permitting transfer of inorganic cations like iron or calcium.^{1,23}

Even after these substances have negotiated the canal system, they still must pass through the syncytial basement membrane which apparently acts as a filter blocking the passage of large particles. Thus, present thinking is that, for a substance to cross the syncytial trophoblast, it must have the ability to avoid being selectively absorbed or structurally modified while in the canal system; then it must successfully cross the basement membrane.¹

Interestingly, no canals or vacuoles such as those described in the syncytial trophoblast have been identified in the cytotrophoblast. Moreover, syncytiotrophoblast of a first trimester placenta seems to have an appreciably less developed canal system. These electron microscopic observations have been used to explain the low gamma globulin concentration in early pregnancy, when there is a complete layer of cytotrophoblast that would presumably impede protein transfer. Overall, the syncytial trophoblast would appear to possess a highly selective and complex transport system which in certain respects might be said to resemble a mammalian renal tubule.¹

In another respect, however, the trophoblast might be likened to pulmonary alveolar tissue. This relates to its function as an intermediary in the exchange of oxygen and carbon dioxide between the maternal and fetal circulations. Believed to play a passive role, term syncytial trophoblast exposed to low levels of oxygen in tissue culture reacted in rather dramatic fashion. The nuclei of the syncytial trophoblast gathered at certain staging areas while the remaining portions had only a thin layer of cytoplasm remaining. Such behavior

was believed to have produced considerable surface areas where there was decided reduction in the distance between the maternal and fetal bloods. Presumably this would then permit an increased oxygen flow rate from mother to fetus. This syncytial trophoblast "accommodation" to hypoxia was reversible if normal oxygen levels were restored to the cultures before exposure time exceeded six hours. The histologic features of this process resembled those found in preeclampsia and usually attributed to "premature aging." Apparently this is more nearly a physiologic adaptive response of the syncytial trophoblast to environmental hypoxia by which oxygen transfer to the fetus might be facilitated.³⁷

Endocrine Function

The appearance, coincident with pregnancy or a trophoblastic tumor, of compounds such as chorionic gonadotrophin, together with their disappearance with the termination of pregnancy or the removal of such placental tumors, led to suggestions that these substances might be produced by placental tissue. Recovery of such substances from placental tissue in prolonged culture promoted the validity of these suggestions. Because placental tissue is composed of different cell types, assigning the cell responsible for the production of these substances could not be done with certainty.

Newer techniques have allowed investigators to attack this problem with less imprecision. One approach involved the use of a rabbit antihuman chorionic gonadotrophin sera which had been labelled with fluorescein. Such a compound would specifically bind to chorionic gonadotrophin. When tissue was viewed by ultraviolet microscopy a typical fluorescence would alert the viewer to the cellular location of such an interaction. This was done in an elegant study by Midgley and Pierce; and the chorionic gonadotrophin, a glycoprotein, seemed to be found exclusively within the syncytial trophoblast cytoplasm of younger placentas and trophoblastic tumors. Curiously, fluorescence was not seen throughout the syncytium but was confined to certain regions. As they pointed out, however, localization of a substance did not necessarily mean production of the substance at that site; it could be that it was stored there.²¹ However, as mentioned previously the syncytial trophoblastic layer has multitudinous submicroscopic organelles which have been interpreted as equip-

ping this cell for specialized functions. Such specialized functions would include the production and secretion of hormones.^{26,27} Taken together, the immunofluorescent and electron microscopic studies have advanced the syncytial trophoblast to be the leading candidate for the production of chorionic gonadotrophin.

Another protein hormone peculiar to pregnancy is chorionic growth hormone-prolactin, also called human placental lactogen. As with chorionic gonadotrophin, the precise purpose of this hormone is not clear although it is thought to be responsible for the maternal resistance to insulin, the so-called diabetogenic effect of pregnancy. However, it, too, has been synthesized by placental tissue in cultures.¹³ Immunofluorescent methods utilizing specifically labelled antisera likewise localized it to the syncytial trophoblast. Unlike the chorionic gonadotrophin, this hormone was apparently distributed diffusely throughout the syncytial cytoplasm of placentas of different stages of pregnancy.³⁰ Current thought also assigns its production to the syncytial cell.¹³

Other tissue culture studies have demonstrated the ability of placental tissue to produce progesterone from nonsteroidal precursors and estrogen from steroidal precursors.³⁴ Certain key enzymes which are necessary for the maintenance of pathways concerned with such steroid metabolism have been demonstrated by histochemical techniques to be confined exclusively to the syncytial trophoblast.¹⁹ These observations have pointed to the syncytial trophoblast layer as being responsible for the production of these steroid hormones.

Present evidence has strengthened the position of the syncytial trophoblast as a hormone production center. Probably there are other hormones still to be identified as being derived from this cell. However, its ability to synthesize two protein hormones, chorionic gonadotrophin and chorionic growth hormone-prolactin, and two kinds of steroid hormones, estrogens and progesterone, already confer upon it a certain peculiarity as an endocrine organ.

Immunologic Aspects

Human pregnancy in its paternal determinants represents a tissue foreign to the mother. Unlike the usual foreign tissue, it is not rejected by the host. Indeed, the human race has thrived under such presumably precarious circumstances. Interest has been directed at this phenomenon in the

hope that such understanding might provide a major insight into the area of tissue transplantation.

Since the trophoblast occupies the intermediate position between the fetal and maternal tissues, it has come under scrutiny in this regard. Much of the work has involved nonhuman test systems and centered about discovering if the trophoblast of certain animal placentas have determinants, histocompatibility antigens, which would provoke an identifiable transplantation-like reaction—that is, a rejection of tissue.

One approach to this problem has involved the placing of fertilized mice ova, embryos or placental tissues beneath the kidney capsules of a different strain of mice. Fertilized mouse ova transplanted at an early stage were found to grow as trophoblast only. The pure growth of trophoblast—in these cases a giant mononucleated cell—was never found to elicit a reaction which was microscopically recognizable as an immunological tissue rejection reaction (homograft or allograft rejection). When the midgestational placenta, which contained other tissues in addition to the trophoblast, and the embryonic tissues were transplanted under the capsule, an identifiable homograft reaction took place.³² Another investigator found that whole mouse placentas did contain paternal components which could provoke a homograft reaction while the trophoblast did not possess these antigens.²⁹ Finally, no extracellular barrier which could interfere with antigen detection by the mother could be identified by ultramicroscopic study of these ectopic implants of mouse trophoblast.³¹ From these studies the opinion was reached that the trophoblast, at least in the mouse, does not have transplantation antigens and therefore is able to serve as a barrier, preventing any interaction which would promote a homograft rejection reaction between the maternal and the fetal organisms.

Another kind of immunological reaction involves the production of circulating or serum antibodies to an antigen stimulus. Such antibodies are identifiable in the beta or gamma globulin fraction of blood. One group of investigators has suggested that a particular globulin appearing in the serum of human mothers soon after delivery might represent a circulating antibody to syncytiotrophoblastic cytoplasm.¹⁶ Indeed, Boss⁵ demonstrated that syncytiotrophoblastic cytoplasm contained antigenic components which initiated the production of circulating antibodies in rabbits.

Furthermore, he demonstrated that certain of these antitrophoblastic antibodies reacted with antigens from the human kidney. However, he could not demonstrate circulating antibodies to these human trophoblastic antigens in the blood of human females in the period immediately after delivery.

On the other hand, human blood group A substance has been localized to the syncytial trophoblast and the cytotrophoblast of human placenta. Curiously, this blood group substance seemed to occur maximally in the trophoblast of the placenta in the early stages of pregnancy.¹² Chorionic villi of placentas delivered at term did not appear to have detectable blood group substance.^{12,35} A parallel situation was found in the fetal tissues: Blood group substances were found in great amounts in the first trimester but disappeared, or almost so, as pregnancy progressed.³³

Another observation of some relevance has been made in cases of chorionepitheliomas. These tumors are the extremely malignant counterparts of placental trophoblast. There are well documented cases in which apparent spontaneous regression of these disseminated tumors in women has taken place as well as numerous cases of complete disappearance of the tumor following certain chemotherapeutic regimens.^{15,24} In comparison, there is a very poor experience both as to regression and chemotherapeutic measures with histologically identical malignant lesions in males. Since most chorionepitheliomas in females derive from pregnancy and are therefore composed of paternal or foreign determinants while male chorionepitheliomas are composed of genetically compatible determinants, an immunologic explanation was proposed. Such an explanation suggests that in females the choriocarcinoma, bearing foreign antigens, provokes an immunologic response. In a small number of cases this response is adequate to erase the offending foreign tissue (chorionepithelioma), while in the majority of cases chemotherapy is a necessary adjuvant to completely swing the balance against the malignant trophoblast. Precisely which immunologic mechanism, if indeed such a mechanism is involved, has not yet been worked out.⁴

The significance of the presence or absence of the various types of antigens on or in the placental trophoblast is at present speculative. Studies have so far failed to supply a convincing immunological link with the causation of preeclampsia, although

trophoblast antigens have been searched for as an etiologic factor.⁵ In contrast, antigenic provocation by early placentas in incompatible ABO matings was suggested not only by the decreased numbers of type A and B children born to type O multiparas¹⁰; but there seemed to be an increase in early abortions occurring in and apparently resulting from incompatible ABO matings.⁹ Still, the essential contribution to the successful survival of the pregnancy appears to depend on the absence of antigens on the cell surface of the syncytial trophoblast which otherwise might provoke a rejection of those fetal tissues.³¹

Migration

Perhaps one of the least understood activities of the syncytial trophoblast is its migration into the circulating blood of the pregnant female. Such capability was initially suggested, just before the turn of the century, by the finding at autopsy of large multinucleated cells lodged in the pulmonary vasculature of gravida; the observation has been repeatedly confirmed.³ This wandering of the syncytial cell was usually believed to be a biologic oddity and idiosyncratic to this cell. In addition, it was felt to be a random occurrence, produced by some manipulative or convulsive episode in the pregnant female which "caused a degenerative loosening of the trophoblast from the villi."²

Reawakened interest in this phenomenon was brought about by the recovery of syncytial trophoblasts from the uterine venous blood and the inferior vena cava blood of females at different stages of pregnancy.^{17,18,36} The cells ranged from 50 to 200 microns in diameter and were found in numbers indicating a deposition rate upwards of 500,000 to 1,000,000 cells per 24 hours during the second and most of the third trimester in normal pregnancy. An apparent diminution in this process took place at or near term. These cells were not recovered from antecubital vein blood of pregnant women, although recently one investigator has purportedly managed to do this.²⁰ Considering the size and the multitude of these cells finding their way into the woman's circulation, such an occurrence does not seem to be haphazard.

The source of these syncytial trophoblasts would appear to be the syncytial trophoblastic layer of the chorionic villus. Formation of these syncytial cells usually takes place at the tip of a villus and involves the assembling of nuclei in cytoplasm which sprouts out from the villus. A constriction

takes place at the base of this sprout, eventually liberating a multinucleated cell. Each of these steps can be seen in cut sections and in tissue culture studies although the continuous process with one sprout has not yet been reported.^{6,14} An impression gained from studying term placental explants is that these sprouts are not a uniform occurrence in all chorionic villi, but vary in frequency according to zonal patterns within the placenta. It seems unlikely that so complicated a process, which probably requires a fair amount of energy, would depend significantly on a traumatic or deteriorative element for its formation.

In proposing that a normal human pregnancy was characterized by an unrelenting shower of inordinate amounts of syncytial trophoblasts into the maternal blood stream, it became necessary to explain the maternal capacity to survive, since these huge cells could serve as emboli and rapidly occlude the pulmonary vascular bed. Required would be a method which could quickly and reliably dispose of these cells with minimal effects on the surrounding tissues or blood components. A clue to such a mechanism was provided by the chance observation that trypsin and plasmin in small concentrations quickly and preferentially broke down the syncytial trophoblastic layer of the human placenta.³⁶ In a parallel finding, partial disruption of the syncytial trophoblast of chorionic villi, with apparent survival of the adjacent mesothelial, endothelial and blood elements occurred when this tissue was explanted into chicken plasma clots and incubated.⁷ Syncytial trophoblasts, therefore, seemed to be peculiarly vulnerable to certain proteolytic enzymes and to a chicken plasma factor which resembled a protease in its action.⁸ Thus, it was hypothesized that a proteolytic mechanism might be available in the maternal organism to account for the clearing of the syncytial cells and avert any pulmonary embarrassment,³⁶ although such an event may occur in cases of large hydatid moles.

At the moment, just what function this continual liberation of syncytial cells serves is conjectural. One notion presumes that the syncytial trophoblast is antigenic and these migratory cells are instrumental in flooding the mother with excessive antigen which interacts centrally with presumed maternal antiplacental antibodies and thereby deprives these antibodies access to the local placental tissues. In such circumstances a state of immunological unresponsiveness would be produced on

the part of the mother toward the placenta and the fetus, allowing the continued tolerance of the pregnancy, which is regarded by some investigators as analogous to a homograft.^{9,36} Another possibility is that this movement of intact syncytial cells from the placental lake to the inferior vena cava and pulmonary vessels, where lysis of the cells occurs, could provide a means of ensuring the release of substances systemically rather than locally. Just what substances this would include is purely speculative. In any case, it is difficult to accept that this syncytial migration is aimless or that it is mechanically induced. Rather, the event appears to be regularly occurring and quite complicated, so much so that it is not hard to look upon syncytial migration as significant and, possibly, crucial for the wellbeing and survival of gestation.

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CASE REPORTS

A Rare Complication Of Sulfadimethoxine (Madribon®) Therapy

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THE INTRODUCTION OF the sulfonamide group of drugs in the late 1930's heralded a new era in the control of infections. Like so many advances, however, these drugs also carried with them several major complications, the most common being blood dyscrasias, crystalluria and jaundice. The search began for newer agents which would be free of these particular complicating problems and as molecular derivatives slowly appeared, toxicity diminished. In 1958, sulfadimethoxine (Madribon®) was made available, offering once-a-day therapy for moderately severe infections. In 1965, Goodman and Gilman¹ stated, "the incidence of hepatitis with the newer sulfonamides is less than 0.1 per cent."

In the present case the first published report of mild hepato-cholestatic jaundice following sulfadimethoxine therapy, the relationship was established by a therapeutic rechallenge.

Report of a Case

A 20-year-old woman, a college student, gave a history of colloid goiter in 1958. She was treated with desiccated thyroid until March 1962 and

had a good response, but in August 1964, thyromegaly was again noted and a small dose of desiccated thyroid was reinstituted. In 1962 the patient came under the care of a dermatologist for the management of facial acne and initially responded satisfactorily to topical therapy. In November 1964, however, this condition flared again and an infective element manifested itself. As a result she was given sulfadimethoxine, 0.5 gm twice a day, beginning 28 November and this dosage was reduced to 0.5 gm daily on 22 December. The therapy was terminated 2 January 1965 in view of satisfactory clearing of the lesions.

The patient was admitted to a hospital 10 June 1965 for surgical treatment of an anal ulcer. Anesthesia consisted of lidocaine (Xylocaine®) and methohexital (Brevital®) following premedication with pentobarbital (Nembutal®), morphine sulfate, hydroxyzine pamoate (Vistaril®) and scopolamine. After operation she received small amounts of morphine sulfate, promethazine hydrochloride (Phenergan®), trimепразine tartrate (Temaril®) and Nembutal.® She was discharged 16 June 1965.

In July 1965 she again had exacerbation of facial acne, and since response to sulfadimethoxine therapy had been good on the previous occasion, the dermatologist reinstituted the agent at a dosage of 0.5 gm twice a day on 27 July. At first she again appeared to do well, but on 11 August she noted dark urine and on 17 August had mild abdominal pain followed by fatigue, anorexia, nausea, vomiting and pruritus with slight loss of weight. When seen on 23 August she had mildly icteric sclerae, normal stools and several scattered enlarged lymph nodes. The liver and spleen were not palpable. In the differential diagnosis, infectious mononucleosis and hepatitis were considered.

Significant laboratory studies were: Hematocrit, 41 per cent; leukocytes 4,700 per cu mm (34 per cent segmented, 1 per cent bands, 62 per cent

Submitted 6 February 1967.

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lymphocytes and 2 per cent eosinophiles and 1 per cent basophiles); heterophile, negative; urine-bile, positive; total bilirubin, 3.4 mg and direct bilirubin, 2.0 mg per 100 ml; serum glutamic oxaloacetic transaminase (SGOT) 550 units; prothrombin time, 76.5 per cent. All medication except desiccated thyroid and therapeutic multivitamins (Optilets®) was discontinued and complete bed rest and dietary restrictions were prescribed. By 31 August 1965 she was much improved and liver function showed decided improvement: Urine-bile, negative; total bilirubin, 1.9 mg and direct bilirubin 0.9 mg per 100 ml; SGOT, 188 units; prothrombin time, 91 per cent; plasma proteins, normal; cephalin flocculation, 2+ (48 hours). She was allowed to return to her studies on 16 September 1965, at which time laboratory findings were virtually normal. The diagnosis at that point was felt to be mild viral hepatitis.

In August 1965, mestranol plus chlormadinone acetate (C-Quens®) was added by the dermatologist as a possible aid to the skin problems. At first the response was good but on 22 January 1966 she was again given sulfadimethoxine 0.5 gm twice a day by the dermatologist to control an exacerbation. The following day nausea and vomiting developed, along with pruritus, dark urine and light stools. The sulfonamide was immediately discontinued and when seen 27 August the patient appeared clinically well.

Laboratory studies on that date gave the following significant findings: Leukocytes, 2,850 per cu mm (segmented 14 per cent, stabs 1 per cent, lymphocytes 85 per cent); urine-bile, positive; total bilirubin 1.8 mg and direct bilirubin 0.8 mg per 100 ml; SGOT, 168 units; prothrombin time, 90 per cent; cephalin flocculation, 2+ (48 hours); alkaline phosphatase, 5.6 Bodansky units; thymol turbidity, 3.6 units. Bed rest was again prescribed and two weeks later all previously abnormal laboratory findings were within normal range.

Comment

Recent contributions to the literature^{1,2,3} have served to point up the fact that sulfonamides can cause hepatic dysfunction, however rarely. The present case is the first reported in which hepatitis followed the use of sulfadimethoxine (Madribon®). The relationship was established by a prompt return of earlier symptoms and laboratory findings when the drug was used a third time. The

laboratory findings suggested a mixed cholestatic-hepatitis response, as evidenced by increased alkaline phosphatase and transaminase. The reaction was clearly mild and readily reversible, and it was more likely a hypersensitivity response than a direct toxic effect of the sulfadimethoxine.

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Lidocaine—*Xylocaine*.®
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Trimethoprim tartrate—*Temaril*.®
Therapeutic multivitamins—*Optilets*.®
Mestranol + chlormadinone acetates—*C-Quens*.®

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Diphenylhydantoin Toxic Psychosis with Associated Hyperglycemia

JAMES R. DAHL, M.D., *San Rafael*

NEARLY 30 YEARS AFTER its introduction, diphenylhydantoin (DPH) (Dilantin®) remains a mainstay in the therapy of epilepsy.¹¹ During this period, its side effects have been well documented. In addition to the well-known, largely dose-related neurologic toxicity,⁸ a number of other complications have been observed, reported and reviewed.¹⁰

The purpose of this report is to describe an episode of transient hyperglycemia and glycosuria associated with DPH toxicity in a non-diabetic patient. No similar cases could be found in a search of the literature.

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Report of a Case

A 47-year-old businessman was first seen 8 September 1965 because of "peculiar behavior" of several weeks' duration. Pertinent medical history consisted of a cerebral concussion at the age of 22, and the onset three years later of grand mal epileptic seizures, which were controlled by treatment with DPH in a dose of 100 mg three times daily. After several years the patient discontinued medical supervision but continued to take DPH. In May 1965, however, he began to feel "peculiar," and fearing that the grand mal seizures were about to recur, gradually increased the amount of DPH taken daily. At the time the present symptoms began, he was taking 700 mg of DPH daily; 500 mg of the daily dose was taken at bedtime. Initially, he noted tinnitus associated with impaired hearing, then ataxia ("shakiness and lurching") and finally delusions regarding his wife's marital fidelity. He began to have visual hallucinations, seeing his wife's alleged lover lurking behind trees and rocks or peering at him from passing cars. At that time he began to carry a loaded pistol, causing his alarmed wife to bring him in for evaluation. The patient's medical and social history was otherwise unremarkable. His appetite had remained good and his diet was normal. He had no family history of diabetes mellitus.

On physical examination, the patient appeared to be in no distress but showed aberrant affect, such as smiling inappropriately or giggling. The blood pressure was 155/85 mm of mercury; the pulse rate was 76 beats and respirations 12 per minute. The only significant abnormalities were found by neurologic examination. He had bilateral fine nystagmus on lateral gaze. Cranial and peripheral motor and sensory nerve function was otherwise normal. Pronounced truncal ataxia was present. The deep tendon reflexes were brisk but equal bilaterally, and the plantar responses were flexor.

Laboratory studies included a hemogram within the normal range. The urine gave a strongly positive reaction for glucose, and a trace of acetone was present. A blood specimen obtained approximately two hours after the patient had eaten lunch showed a glucose level of 230 mg per 100 ml (Table 1).

The dosage of DPH was immediately reduced to 200 mg daily. When the patient was seen two days later, the symptoms and neurologic abnormalities had all but disappeared. Glycosuria was no longer present, and the fasting blood glucose level was normal at 100 mg per 100 ml. These findings suggested that the hyperglycemia and glycosuria were related to DPH toxicity. Blood glucose determinations including a cortisone glucose tolerance test to detect mild carbohydrate intolerance² were performed during the subsequent eight months. The results (Table 1) documented the recovery of normal carbohydrate regulatory function.

Within one week of the first office visit, the patient became free of symptoms and neurologic abnormalities and has remained so to the present. Blood pressure levels have ranged between 145/85 and 160/90 mm of mercury. He has continued to take DPH in a dosage of 300 mg daily.

Discussion

As is apparent from Table 1, the patient's blood glucose level became normal in the fasting and two-hour post-glucose state after his recovery from DPH toxicity. A cortisone glucose tolerance test was then performed because of the possibility that he might have "pre-clinical" diabetes. Although the results were abnormal by the original criteria of Fajans and Conn,² the patient ranked in the 25th percentile of the nomogram constructed by Pozefsky and co-workers⁶ to allow comparison of the test values in a given patient with those of his age cohorts, which is well within

| | Date | Determination | Blood Glucose Levels* (mg per 100 ml) | | | | |
|--------------------------------------------------------|----------|-------------------------------------|------------------------------------------|---------|-------|-------|-------|
| | | | Fasting | 30 Min. | 1 Hr. | 2 Hr. | 3 Hr. |
| TABLE 1.—Results of Blood Glucose Determinations | 9/ 8/65 | Random, 2 hours after lunch..... | | | | 230 | |
| | 9/10/65 | Fasting | 100 | | | | |
| | 9/15/65 | Partial glucose tolerance test†.... | 80 | | | 120 | |
| | 10/28/65 | Cortisone-glucose tolerance test‡ | 114 | 236 | 240 | 180 | 140 |
| | 5/ 5/66 | Random | | | | 118 | |
| | 5/11/66 | Standard glucose tolerance test† | 70 | 120 | 140 | 100 | 88 |

*Folin-Wu; normal fasting level, 80-120 mg.

†Glucose, 100 gm orally, after fasting sample is taken.

‡Hydrocortisone, 50 mg orally, 8½ and 2 hours before administration of glucose.²

their normal range. Finally, eight months after the initial episode a standard glucose tolerance test gave normal values.

It thus appears that the hyperglycemia and glycosuria observed in this patient were related to the DPH toxicity and were mediated by a mechanism other than that operating in the stressed "pre-diabetic" subject. Several possibilities seem to exist. Release of ACTH has been reported to be inhibited³ and plasma 17-hydroxycorticoid levels low or normal¹ in patients receiving DPH, so it seems unlikely that the pituitary-adrenal axis mediated the observed effect. Epinephrine infusion has been shown to inhibit release of pancreatic insulin,^{4,5} thereby potentiating the hepatic glycogenolytic hyperglycemia also induced. Not to my knowledge, however, has the production of sustained hyperglycemia via this mechanism been documented in acutely stressed patients.

Finally, a direct effect of DPH on the pancreatic release of insulin can be postulated. Woodbury¹² suggested that DPH exerts its anticonvulsant action by diminishing the intracellular sodium content of the brain, thereby lowering excitability. He also noted the stimulating effect of DPH on cellular sodium-extruding processes in cardiac and skeletal muscle. This observation is of interest in view of the well-known hyperglycemic effect of the thiazide diuretics.⁹ The mechanism of their hyperglycemic action remains unclear, but intracellular potassium depletion appears to be a possible explanation, at least in part.⁷ It is thus tempting to speculate that the effect of DPH in the present case was similarly mediated via an induced alteration in the electrolyte concentration of the pancreatic islet cells, thereby inhibiting insulin secretion.

Summary

The occurrence and remission of hyperglycemia and glycosuria in conjunction with diphenylhydantoin (DPH) toxicity in a non-diabetic patient is described. No similar cases were found in the literature. An inhibitory effect of DPH on insulin secretion by the pancreatic islet cells is one of several possible explanatory mechanisms.

GENERIC AND TRADE NAME OF DRUG

Diphenylhydantoin—*Dilantin*.®

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Gynecomastia Associated with Vincristine Therapy

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Vincristine (Oncovin®), a chemotherapeutic agent derived from the periwinkle plant (*vinca rosea* Linn), has been demonstrated to induce remissions in various neoplastic diseases including myeloproliferative and lymphoproliferative syn-

This material has been reviewed by the Office of The Surgeon General, Department of the Army, and there is no objection to its presentation and/or publication. This review does not imply any indorsement of the opinions advanced or any recommendations of such products as may be named.

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dromes.¹ Adverse reactions to the drug are common, with neurologic deficits predominant in frequency and severity.³ While using vincristine we observed a previously unreported side effect, gynecomastia, which occurred in two of twenty adult male patients receiving this drug for four weeks or longer.

Reports of Cases

CASE 1.—A 30-year-old white man, previously normal except for unilateral testicular atrophy associated with varicocele, was found to have stage III Hodgkin's disease in September 1963. During the ensuing year he received repeated courses of radiation therapy and three courses of nitrogen mustard therapy. Upon exacerbation of the disease, he was treated with weekly intravenous injections of vincristine from December 1964 to March 1965. On 8 February 1965, after four doses of vincristine, 0.04 mg per kg of body weight per week, gynecomastia was noted in the form of a 2×4 cm tender, hypertrophied mass beneath the areolar area of the right breast. The dosage was halved at that time, but two weeks later the opposite breast was similarly involved. One month later, despite continuing therapy, the masses had decreased in size. Following discontinuation of the drug at the end of March, the masses were smaller and nontender. Subsequently, the masses disappeared, although the patient's clinical course indicated continued activity of Hodgkin's disease.

CASE 2.—A 57-year-old Malaysian man was found to have reticulum cell sarcoma upon biopsy of a left cervical mass in July 1964. The cervical areas bilaterally and the mediastinum were treated initially with radiation. The abdomen was also irradiated after resection of an obstructing cecal lesion in February 1965. By early April 1965, a right cervical mass was noted. The patient was dysarthric and had a right cranial nerve palsy. On 23 April, vincristine therapy was begun in a dose of 0.025 mg per kg of body weight per week. By 24 May, paresthesias had developed in both hands and there was a tender 4×4 cm mass beneath the areola of the left breast. Significantly, the dysarthria improved and the neck mass decreased in size. By 22 July both breasts contained firm, tender, hypertrophied subareolar tissue and on biopsy of the mass in the left breast the typical histologic features of gynecomastia were seen. Urine 17-keto and 17-hydroxy corticoid deter-

minations as well as gonadotropin determinations were within normal limits. By 30 August, despite continued treatment with vincristine, the breast masses had decreased in size and subsequently they disappeared. The patient remained well while receiving vincristine therapy, without evidence of tumor recurrence or gynecomastia.

Discussion

Gynecomastia is defined as an enlargement of the male breast with round cell infiltration, proliferation of connective tissue and mammary ducts and absence of encapsulation.⁶ It is manifested clinically by a tender mass underlying the nipple and areola and may be associated with secretion of colostrum. This condition is to be distinguished from mammoplasia, occurring in adolescent and senescent males, in which the tenderness and chronic inflammatory infiltration is lacking.²

A list of medications associated with gynecomastia previously reported is tabulated in Table 1.^{4,5} We were unable to find reports of gynecomastia associated with either Hodgkin's disease or reticulum cell sarcoma, although actual tumor invasion has been reported with these and other malignant diseases. Repeated careful evaluation of the two patients in this report failed to reveal any other apparent cause of gynecomastia. Development of the condition several weeks after the beginning of vincristine therapy strongly suggests a casual relationship with drug administration. This annoying, but minor, side effect appears to be transient in nature and may disappear during continuation of therapy.

Summary

Bilateral gynecomastia developed in two men while they were receiving vincristine therapy for malignant disease. In one case, biopsy showed the lesion to be histologically typical of gynecomastia. The condition was transient, the lesions subsiding despite continuation of therapy. These two cases

TABLE 1.—*Drugs and Hormones Associated with Development of Gynecomastia*

| | |
|----------------------|----------------------------|
| Estrogens | Gonadotropins |
| Androgens | Anterior pituitary extract |
| Desoxycorticosterone | Amphetamines |
| Digitalis | Reserpine |
| Isoniazid | Radioiodine |
| Griseofulvin | Oleandomycin |
| Spirolactone | Tetracycline |
| Progesterone | |

suggest that gynecomastia may appear as a side effect of vincristine therapy, that it is transient in nature and that breast enlargement during such therapy need not be considered evidence of neoplastic involvement.

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Lactose Intolerance

These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California Medical Center, San Francisco. Taken from transcriptions, they are prepared by Drs. Martin J. Cline and Hibbard E. Williams, Assistant Professors of Medicine, under the direction of Dr. Lloyd H. Smith, Jr., Professor of Medicine and Chairman of the Department of Medicine.

DR. FOURCADE*: The patient is a 38-year-old nurse who was admitted to this hospital because of intermittent diarrhea and abdominal pain for the past nine years, increasing over the past one year. She has had ten to twelve bowel movements a day during this period. The stools were described as loose, watery, brown, foul smelling, and occasionally greasy or foamy, sometimes floating. The patient described the abdominal pain as cramping in nature, occurring one to two hours after meals. She also noted that milk caused some abdominal discomfort. In the past year her weight had decreased approximately 15 pounds. She had had no weight loss during the preceding eight years. Three intra-abdominal surgical procedures were confined to pelvic organs. The patient denied bone or joint pain, fever or jaundice. Cultures of the stool have been negative in the past and treatment with corticosteroids for three months was without effect on either diarrhea or pain.

On physical examination the patient was observed to be slim, well-nourished and depressed but in no acute distress. The vital signs and results of the examination of the skin, eyes, tongue, chest and heart were within normal limits. Examination of the abdomen revealed diffuse tenderness but no masses or organ enlargement. Results of blood cell count and urinalysis were within normal limits. Results of all other studies of the feces including examination for occult blood, ova and parasites, were negative. Studies for malabsorption also were negative.

No rise in blood glucose was observed after the patient ingested first 50 grams and then 100 grams

of lactose, whereas with similar doses of glucose, galactose and sucrose a normal rise in blood glucose was observed. About two to six hours after ingesting the lactose, the patient noted severe diarrhea and cramps. Biopsy of the jejunum was attempted but insufficient tissue was obtained. The patient was discharged and appeared more comfortable on a lactose-free diet.

DR. ZBORALSKE*¹: Two upper gastrointestinal and small bowel series were performed. The first of these (Figure 1), using a barium preparation which does not contain sugar, was within normal limits. Contrast material did appear in the colon within 30 minutes, suggesting rapid transit. However in some normal patients barium will appear in the colon within 30 minutes and this cannot be considered unusual. There was no dilatation of the bowel and the barium was dispersed throughout.

Twenty-four hours later the patient was given barium containing 50 grams of lactose. In this study (Figure 2) the small bowel is dilated, and the normal valvular pattern is lost. There is homeogeneity, which suggests increased fluid within the lumen of the small bowel. From the study with lactose there appears to be an increased amount of fluid within the lumen and there is some dilatation of the small bowel, jejunum and ileum.

DR. SMITH*²: Thank you, Dr. Zboralske. This patient, unfortunately, is not here for presentation in person this morning. She was referred to the hospital by Dr. Harry Daniel and Dr. Howard

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*²Lloyd H. Smith, Jr., M.D., Professor & Chairman, Dept. of Medicine.

*Henry E. Fourcade, M.D., Resident in Medicine.



Figure 1.—X-ray film with barium preparation (without sugar).

Shapiro. I wonder if they would care to comment before the main discussion.

DR. SHAPIRO^{*3}: I have no comments to make except to remind everyone concerned that three years ago this patient might have been given the diagnosis of psychogenic diarrhea.

DR. SMITH: This is an intriguing subject which has been prominent in the medical literature in recent years, with increasing understanding of disaccharide intolerance. We are very fortunate to have Dr. Keith Taylor with us today to lead the discussion concerning this patient and this interesting syndrome. Dr. Taylor was originally from England and had his undergraduate and medical training at Oxford University. He is now at Stanford University as Professor of Medicine and chief of the Gastroenterology Section. Dr. Taylor.

DR. TAYLOR^{*4}: Thank you, Dr. Smith. When I was asked to lead the discussion about this interesting patient I explained to Dr. Smith that I was not active, myself, in the exciting field of disaccha-

ridase deficiency and of intolerance to disaccharides. It is one which is developing so rapidly that many of us find the wealth of material presented in the literature somewhat indigestible. A few years ago one would not have considered the question of disaccharide intolerance at all in a patient of this sort. Now perhaps the pendulum is swinging a little too far the other way. I suppose that ultimately we shall find some middle course; this will depend on our capacity to relate available data to any particular patient presenting in this way. Major deficiencies of most studies in this area are the lack of control data, particularly disaccharide tolerance curves and enzyme estimations in jejunal and lower intestinal material, and proper correlation of these parameters with the clinical picture in various groups of patients.

The problem posed by this patient is: "Are her symptoms really caused by a failure specifically to handle lactose?" In order to answer this, we need a few hints in the history; first, are her symptoms brought on by the ingestion of lactose? As you know, in the past, many patients in whom intolerance to milk was reported were thought to have allergic sensitivity to milk proteins. It is only in recent years that the problem of lactose intolerance has been raised. The second question is: "Are her symptoms relieved by exclusion of lactose from the diet?" The patient has had symp-



Figure 2.—X-ray film with barium containing 50 gm of lactose.

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toms for nine years, gradually increasing in severity and much worse in the last year. There has been loss of weight and a change in her bowel habit, resulting first in intermittent and later in continuous diarrhea. Does lactose exclusion relieve this? Since the patient was observed to be "depressed," it is difficult to interpret the response to the changes in diet, which were not evaluated by double blind technique. I think this is something we have to consider very seriously in someone with a problem of this type. Thirdly, we have the results of tolerance tests, which could be interpreted as showing a deficiency of lactase activity in the bowel. Finally we would like to have evidence of lactase deficiency by small bowel biopsy, which was quite properly attempted but which did not succeed.

At this point we might consider one or two problems relating to disaccharide absorption and then return to this patient. The problem under consideration today involves the method by which lactose is handled, but other disaccharidases, such as maltase and iso-maltase, are important and might be considered also. When lactose is ingested, it may either be unabsorbed, pass on and be fermented in the lower part of the bowel, or it may be converted to glucose and galactose and transported across the intestinal wall into the blood. In certain situations, particularly in very young children, free lactose may be absorbed and appear in the blood as lactose. When compared with other disaccharidases, lactase, which is a very specific enzyme, is probably present in lowest activity in the gut wall, and perhaps therefore may be most susceptible to any injury, toxic or mechanical. Recent work suggests that two lactases exist and at the moment it is not known whether one or both play a part in lactose digestion.

The exact location of these enzymes has been studied in a number of different ways. Perhaps the nicest demonstrations have been those of Crane and his coworkers in Chicago, who devised a beautiful technique for separating various fractions of the epithelial cells of the small intestine, using ethylene diamine tetraacetic acid (EDTA) buffers. With this method they disrupted the epithelial cell, retaining intact, or apparently intact, the brush borders—that part of the cell that contains the micro-villi and the immediate adjacent structures. These investigators demonstrated that the major part of the activity resides in the components of the mucosa which are found deeper in the villi. The most superficial parts of the tips of

the villi contain maximal disaccharidase activity. In the deeper layers of the epithelium, the deeper layers of the villi and in the crypts the activity is reduced. This has been demonstrated also with labelled antibodies directed against specific disaccharidases, which are taken up by the brush borders of the small intestinal epithelial cells. This kind of evidence suggests very strongly that this location is the site of the highest concentration of the enzymes, the site of hydrolysis of disaccharides. This has been shown also by various labelled sugar experiments.

For years, particularly in children, the concept of fermentative diarrhea has been entertained. Certain children appear to tolerate sugars poorly, as manifested in diarrhea, weight loss and other symptoms. The first breakthrough was by Holzel and his colleagues in an important and now historical paper. These investigators showed for the first time that in a number of children with intolerance to disaccharides, particularly lactose, a flat lactose tolerance curve could be demonstrated. The idea grew from Holzel's work that these findings were due to lactase deficiency in the gut wall and that fermentative diarrhea of this type might be associated with a lactase deficiency. However, for some time, Holzel insisted that these were in fact two different types of intolerance to lactose in infancy. One type, which he described as lactose intolerance, was associated with lactosuria, with a normal lactose tolerance curve and severe symptoms with ingestion of lactose. The second type represented a deficiency of lactase in the gut wall, and was associated with milder symptoms and absence of lactosuria. More recently, this separation has not been endorsed, and many investigators in this field today, I believe, would consider the idea of lactose intolerance specifically in terms of lactase deficiency.

The syndromes associated with lactose intolerance are many. Congenital lactase deficiency, occurring in infants, with or without lactosuria has been mentioned. Several questions about this syndrome arise. Is this truly congenital? Is it ever familial? Is it in fact genetically determined? The present evidence is extremely difficult to interpret. Studies in this field have been so few in total number that it is extremely difficult to dissociate environmental factors from genetic factors, and at the moment this point seems to be unproved.

Secondary lactase deficiency includes a number of clinical situations: Lactase deficiency in association with intestinal infection, which has been

observed frequently in children and appears to be quite non-specific; lactose intolerance associated with malnutrition, particularly in infants; and that seen in association with gross changes of the intestinal mucosa produced by gluten-induced enteropathy. In these latter conditions there is in fact lack of many disaccharidases, and lactase particularly is the enzyme most deficient.

After extensive small bowel resection a reduction in the total amount of lactase is expected and the distribution of lactase along the gut seems to be an important factor. One may expect to find low lactase activity at the region of the ligament of Treitz. This activity is well maintained throughout the first half of the small intestine, but with some tendency toward diminution in the distal part of the small bowel. This is a very important point in deciding where to take a specimen for biopsy and what interpretation to place on the biopsy observations.

The question of lactose intolerance associated with milk intolerance in adults is a difficult one. The best way to dissociate the intolerance toward milk due to protein sensitivity and that due to lactose intolerance, is to determine by a series of feeding experiments, preferably done by double blind techniques, that only lactose will produce symptoms and milk proteins *per se* will not do so. A useful source of milk protein is cheese, which contains little lactose. In the future the use of purified milk protein may help to differentiate these two possibilities.

Next is the question of lactose intolerance in association with chronic inflammatory disease of the bowel, both of the small bowel and of the large bowel. There have now been a number of studies reporting diminution of enzyme activity in these various diseases. The role of this disaccharidase deficiency, either in the continuation of the disease or exacerbation of the disease process, is uncertain. Again we still lack sufficiently well controlled studies. Lactose intolerance may also occur in cystic fibrosis, in severe infestations with *Giardia*, and with beta-lipoprotein deficiency. Finally we have the recent observations that lactase deficiency may develop in the gut wall of women taking oral contraceptives, and disappear when use of these steroids is discontinued.

A number of factors will affect the activity of lactase in the bowel wall. First, the question of age. There seems to be in fact some minor variation with age (although this is much more appar-

ent in certain laboratory animals who show very clear evidence of a decrease in lactase after weaning). This is not nearly so apparent in man. The next question relates to the expression of enzyme activity—the units of lactase activity. This activity relates to the rate of destruction by hydrolysis of the appropriate substrate in terms of micromoles released at 37°C, expressed in relation to the weight of the tissue which contains the enzyme. This is usually in terms of wet weight of the tissue, but some investigators have used dry weight, and some others have used protein content as a reference. This leads to some confusion and there is little agreement at the moment as to which is the most appropriate reference to use.

Next the question of race and environmental factors has to be considered. It has been shown recently in Africa that intestinal lactase activities in adjacent tribes is quite different, and at the moment this has not been related fully to any particular dietary habits. Yet these tribes are quite close ethnically. One study of lactose intolerance included a mixed group of Caucasians and Negroes. Negroes were apparently symptom-free but had low enzyme activity. This suggests that there may actually be racial differences in enzyme activity.

The question of diet has not been resolved. Some evidence exists in animals that diet can induce changes in the concentration of these enzymes, particularly of lactase. There is no evidence as yet that suggests this situation in man.

The question of tolerance curves then arises. The early demonstration by Holzel and others suggested that in the absence of diabetes a flat lactose tolerance curve indicated a lactase deficiency in the gut. There was no biopsy confirmation. Attempts have been made to correlate the enzyme activities and the lactose tolerance curves. At first good correlation was apparent. It was also noted that some patients who were asymptomatic would have both flat lactose tolerance curves and hypolactasia defined by multiple observations. However, more recently there have been a number of studies to show this is no longer true. In a recent study, 16 patients with normal gastrointestinal function were given both 50 and 100 gm lactose loads by mouth. Three of these 16 patients had an increase in blood glucose of less than 10 mg per 100 ml following ingestion of the lactose. Yet biopsy specimens from these patients showed no deficiency of lactase. This suggests that we still

need to know a great deal more about the actual correlation of lactose absorption and the activity of lactase in the gut.

We come finally to the studies which have been done on lactase activity in biopsy material. Here again the initial studies looked extremely encouraging, with good correlation between clinical symptoms and lactase activity in the gut wall. However, recently it has been shown that many persons who appear to have hypolactasia have no symptoms, either with a normal diet or with lactose ingestion. Furthermore some control subjects have been found to have very low or absent lactase activity in the gut wall but no symptoms.

It is with patients similar to the patient presented today that we are very much concerned. The question now remains as to whether her symptoms are due to lactose intolerance and in turn to hypolactasia, or are the data which have been obtained explicable in other ways—such as changes in gastric emptying, changes of intestinal transport, or other diseases of the gastrointestinal tract which have not yet been found. I must confess I found the x-ray films extremely impressive—an excellent demonstration of a response to lactose in the barium solution. Did the patient know that lactose was present? I feel I must ask you that at this stage.

DR. FOURCADE: Yes, she did know that lactose was being added. Also of importance is the fact that we did not have an opportunity to test some normal subjects.

DR. TAYLOR: This question is very important. Gastric emptying can be delayed with hypertonic solutions in the stomach. This may explain why the use of 50 gm and 100 gm lactose loads may give divergent results in subjects studied with both doses. Some patients show a higher peak of blood glucose after 50 gm and some show it after 100 gm. This can really only be explained in terms of the weight of material presented to the gut wall. Another point is that many of us find the taking of hypertonic solutions nauseating, as I did the first time I took 25 gm of xylose.

Why does lactose produce diarrhea, if it does? The possibilities include a lower pH and probably increased lactic acid in the stool. In some patients

the colon seems to do a good job of removing the lactic acid, and one may not always find this in established cases of lactose intolerance. It is conceivable that lactose affects the flora of the gut in some way.

I think I have said quite enough, Dr. Smith. I have said nothing which would allow any firm diagnosis to be made in the patient presented but I hope I have stimulated thinking about these problems. The days when the gastroenterologist could just talk about the irritable bowel syndrome and nervous diarrhea appear, fortunately, to be coming to an end. Thank you very much.

DR. SMITH: I think Dr. Taylor has given us an excellent summary of this complex subject, and also in a very quiet and gentle way has let us know that our evidence is inadequate to support the diagnosis listed in the protocol. I would like to throw this open for discussion and comment.

DR. WILLIAMS^{*5}: Since the pH optimum of most of the disaccharidases is close to 6.5, does the pH of the bowel contents affect enzyme activity?

DR. TAYLOR: I think this is an extremely important point, and it may help us to explain why primary disturbances of the bowel may lead to observed intolerance in the handling of lactose. But I do not think we have adequate measurement of local pH conditions in the bowel. Perhaps with new telemetering devices we shall obtain more information about pH.

PHYSICIAN IN AUDIENCE: There is apparently some evidence that the severity of symptoms with lactose is proportional to the amount of ingested lactose. Do you feel that the 100 gram test offers sufficient stress to bring out a flat curve?

DR. TAYLOR: I think it would be very difficult to administer more than 1.5 gm per kg of body weight, which is about as much lactose as anyone can tolerate. No one, so far as I know, has pursued this further, as has been done for fat ingestion; that is, to gradually increase the quantity of lactose until absorption levels off and an excess appears in the stool. I am not aware of any studies of that sort, but I would be pleased to hear of them.

^{*5}Hibbard E. Williams, M.D., Assistant Professor of Medicine.

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DWIGHT L. WILBUR, M.D.

Assistant to the Editor
ROBERT F. EDWARDS
For information on preparation of
manuscript, see advertising page 2

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EDITORIAL

For New Directions, New Directors

IN THE APPOINTMENT OF a new editor and associate editor (see page 356) to succeed Dr. Dwight L. Wilbur, who has resigned effective next 1 January, the Council of the California Medical Association has chosen wisely a team nicely balanced in scientific stature, familiarity with the functions of the association, administrative ability, attainment in academic fields, interest in continuing medical education, private practice and grounding in the editorial work of a medical journal.

The special committee of the Council that was set up for the purpose was guided by these considerations—and by the fact that the publication office of the journal is in San Francisco—when it recommended Dr. Malcolm S. M. Watts and Dr. Lloyd Hollingsworth Smith, Jr., for editor and associate editor respectively.

Between them—and overlapping in considerable degree—Doctors Watts and Smith have the high standing in the academic world, the reaches into sociologic and political understanding, the organizational and administrative talent, the indoctrination in the purposes of our state medical association and the interest in private practice that can combine to direct CALIFORNIA MEDICINE into the changing channels it must follow as a representative function of an organization whose record is peerless among state medical associations in its concern with socio-economic matters,

its relationships with governmental bodies, its fervor for continuing medical education and its active promotion of the best in health care.

Now recognized as outstanding among state medical journals, CALIFORNIA MEDICINE must progress as an instrument of communication and education to reflect the increasing importance of its area in the field of medical education, the growing number and quality of medical schools, the greater sophistication of medical practice and the burgeoning of interest in continuing medical education.

The new appointees come to the work of the official journal of the California Medical Association at a time when it has reached a plateau characteristic of the provincial limits of state journals. We look forward to the ideas and fresh enthusiasm that the new editors can bring to the job of shaping CALIFORNIA MEDICINE to fit the rapidly changing circumstances of medical practice and teaching in this part of the country. And we may expect that, as the primary directors of a scientific publication in a state that is rich in facilities for medical education and is the biggest of a group of states which also have medical schools, this new team may begin to look beyond the nominal boundaries of a state journal for editorial material and for readers.

California Medical Association



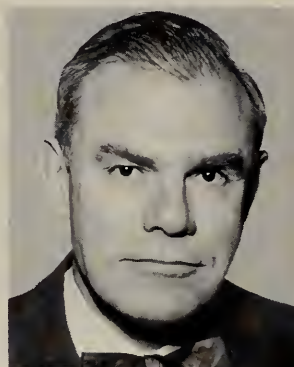
NOTICES AND REPORTS

New Editor and Associate Editor

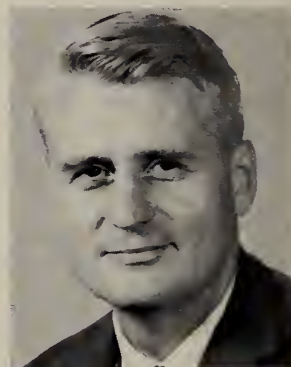
DR. DWIGHT L. WILBUR HAS RESIGNED the editorship of CALIFORNIA MEDICINE, a post he has held since May 1946, because of the press of work associated with his election as President-Elect of the American Medical Association, and the Council of the California Medical Association has appointed a new editor and an associate editor. The resignation and the new appointments are effective 1 January 1968.

The new editor is Dr. Malcolm S. M. Watts and the associate editor Dr. Lloyd Hollingsworth Smith, Jr., both of San Francisco. They were appointed upon the recommendation of a special committee of the Council under Dr. Wilbur's chairmanship.

Dr. Watts, an internist in private practice and a member of the CMA Council, is also on the



Malcolm S. M. Watts, M.D.



Lloyd H. Smith, Jr., M.D.

teaching and administrative staff of the University of California School of Medicine, San Francisco, currently as associate clinical professor of medicine, associate dean of the medical school and special assistant to the chancellor. In the California Medical Association he has served on a number of important committees and commissions, among them the Scientific Board, the Public Relations Committee, the Committee on the Role of Medicine in Society, the Bureau of Research and Planning and the California Committee on Regional Medical Programs. He is a past president of his county medical society. The new editor has published a number of articles both on scientific and sociologic aspects of medicine. His undergraduate schooling was at Harvard College and his degree in medicine is from Harvard Medical School, 1941.

Dr. Smith is professor of medicine and chairman of the Department of Medicine, University of California San Francisco Medical Center, and physician-in-chief of the medical staff of University of California Hospitals, San Francisco. He

| | |
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has been in research and teaching almost continuously since he received his M.D. degree from Harvard Medical School in 1948. His undergraduate schooling was at Washington and Lee University. Dr. Smith, whose association with CALIFORNIA MEDICINE began in 1966 with his supervision of the Medical Staff Conferences published monthly in this journal, has a groundwork of experience in editorial work. He has written extensively and is a member of the editorial boards of *The Journal of Clinical Investigation* and the *American Journal of Medicine*.

Both of the appointees are at work with plans and the review of material that will appear in CALIFORNIA MEDICINE after they officially take office 1 January.

Where We Stand on Drug Abuse

ONE OF TODAY'S MAJOR social problems is the rapidly growing and indiscriminate use of drugs. The problem is particularly acute with our young people. Since the medical profession has responsibility of treating conditions arising from the misuse of certain drugs, it therefore feels an obligation to state its position on this matter and offer counsel to those who are concerned with this increasingly grave problem.

The use of drugs in the practice of medicine is centuries old. Modern medical practice has found that many different drugs and drug derivatives are indispensable tools to the treatment of mankind's many ills. Indeed, there are few households in our country today who do not have a well-stocked medicine cabinet containing one or another of the thousands of prescriptive medicines derived from raw or synthetic drug products. New advances in drug research have spectacularly eradicated diseases which were the scourges of previous eras. Is it any wonder then that some sociologists refer to today's society in terms of a "drug culture"?

But we know that drugs taken indiscriminately and without proper medical guidance can also have an adverse effect. And it is to this problem that we direct ourselves in this paper.

The Definition

Drug abuse is a complex constellation of related, but different problems. The boundaries are

not distinct, and often coexist in the individual. Drug abuse has been defined in many ways. The State of California Department of Education, for example, adopted the definition "a drug may be said to be abused when it is obtained illegally or self-administered to the possible detriment of the individual, of society, or of both." Others might restrict the term to narcotics, addictive dangerous drugs or psychedelic drugs. Drug abuse, to some, includes all forms of drug intake, which may have an adverse effect on health. Cigarettes, coffee and alcohol are some of these drugs. Other than realizing this diversity of opinion, formal widely agreed definition is not needed.

The magnitude of the problem varies. The problem of hard core narcotic addiction (opiates) seems to be decreasing. All other forms of drug abuse seem to be increasing both in number and public concern.

The drug problem must be considered in four main categories: The dangerous drugs (narcotics), stimulants and depressants (amphetamines, barbiturates, etc.), psychedelics (LSD, DMT, etc.) and marijuana.

Narcotics, we can state without reservation, are dangerous, addictive and illegal and should only be used under rigid controls. An unfortunate number of people have found this out to their lasting regret. Effective law enforcement, intensive medical treatment and enlightened public awareness of the dangers of these narcotics have contributed to a measure of control.

However, it is with the other three categories that we now find ourselves faced with a severe and growing dilemma. The use of stimulants, psychedelics and marijuana has become widespread among our youth.

Some social thinkers speculate that this increasing misuse is a symptom of social insecurity, psychological pressures of contemporary living, unproductive leisure time and uncertain drift in the spiritual sustenance of life.

Our Position

1. The California Medical Association does not have the scientific facts, nor unanimous opinion of its members, to recommend major legislative changes related to drug abuse at this time.

Medicine's position in relation to drug use must, of course, be determined in relation to the law as it exists today. All opium derivatives, as well as marijuana, the amphetamines and the so-

Adopted by the Council, 27 August 1967.

called psychedelics are strictly controlled through prescription requirements and by statute.

Extra care must be maintained in the control of psychedelic drugs which seem to require more concerted and reasoned action by the entire community, because legal prohibition alone does not seem to have been sufficient and may even have driven the problem further underground.

2. The California Medical Association and other allied health agencies should continue to sponsor and cooperate in studying the magnitude, causes, and control of drug abuse.

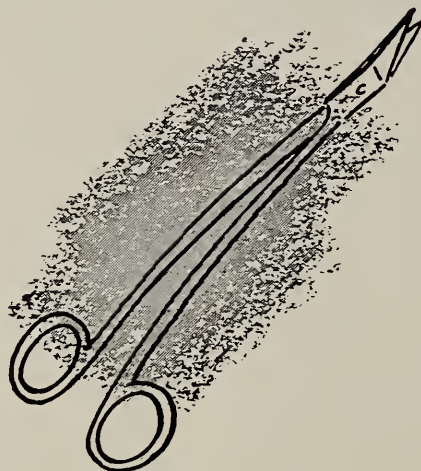
3. The medical profession, by its training and experience, is particularly aware of the potential danger of new drugs, especially those without rigid control studies by competent scientists.

4. Until further scientific evidence is available to prove or disprove the value of marijuana and the LSD compounds, the California Medical Association adopts as its official position the following statement made by Dana L. Farnsworth, M.D., Director, and Curtis Prout, M.D., Chief of Medicine of the Harvard University Health Services:

"Marijuana does not produce physical addiction, but it does produce significant dependence, to a serious degree. This is a fact well known to doctors working with college students. The social influences surrounding the use of marijuana also encourages experimentation with other drugs, notably LSD, and, of course, may lead into addiction to narcotics.

"We know now that long-term subtle psychological damage may result from LSD. Such damage may be glossed over by the pleasure and enthusiasm engendered by the substance, but we have seen too many cases of psychic breakdown to doubt the serious dangers of the drug. It is even possible that the brain is structurally damaged. There is recent evidence that LSD attacks hereditary genes.

"In short, our professional medical opinion is that playing with LSD is a desperately dangerous form of 'drug roulette.' The medical evidence is clear. Any person taking LSD runs the clear risk of psychotic breakdown and long-run physiological damage."



❧ In Memoriam ❧

BALL, FRANKLIN I., Los Angeles. Died 21 August 1967 in Los Angeles of heart disease, aged 61. Graduate of the University of Oregon Medical School, Portland, 1931. Licensed in California in 1933. Doctor Ball was a member of the Los Angeles County Medical Association.



CARPENTER, LAWRENCE O., Santa Rosa. Died 31 July 1967 in Santa Rosa, aged 44. Graduate of Western Reserve University School of Medicine, Cleveland, Ohio, 1949. Licensed in California in 1955. Doctor Carpenter was a member of the Mendocino-Lake County Medical Society.



FUCHS, ARTHUR ROBERT, Long Beach. Died 7 August 1967 in Long Beach of cerebral vascular disease due to hypertension, aged 63. Graduate of Johann Wolfgang Goethe-Universität Medizinische Fakultät, Frankfurt-am-Main, Prussia, Germany, 1927. Licensed in California in 1944. Doctor Fuchs was a member of the Los Angeles County Medical Association.



HOWARD, HARRY EMERSON, Danville. Died 11 August 1967 in Walnut Creek of coronary atherosclerosis, aged 42. Graduate of the University of Michigan Medical School, Ann Arbor, 1948. Licensed in California in 1950. Doctor Howard was an associate member of the Alameda-Contra Costa Medical Association.



HOXIE, HAROLD JENNINGS, Glendale. Died 20 August 1967 in Glendale of cancer, aged 59. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1933. Licensed in California in 1933. Doctor Hoxie was a member of the Los Angeles County Medical Association.



MEADOFF, NATHAN, Bakersfield. Died 29 August 1967 in Bakersfield, aged 54. Graduate of the University of California School of Medicine, Berkeley-San Francisco, 1938. Licensed in California in 1938. Doctor Meadoff was a member of the Kern County Medical Society.



POLLOCK, WAYNE EVANS, Sacramento. Died 4 September 1967 in Sacramento, aged 65. Graduate of Stanford University School of Medicine, Palo Alto-San Francisco, 1928. Licensed in California in 1928. Doctor Pollock was a member of the Sacramento County Medical Society.

POTKIN, CARL, Los Angeles. Died 12 August 1967 in Los Angeles, aged 57. Graduate of Chicago Medical School, 1935. Licensed in California in 1955. Doctor Potkin was a member of the Los Angeles County Medical Association.



RICHEY, THEODORE WESLEY, Santa Barbara. Died 17 April 1967 of myocardial infarction, aged 43. Graduate of the University of Kansas School of Medicine, Lawrence-Kansas City, 1952. Licensed in California in 1957. Doctor Richey was a member of the Santa Barbara County Medical Society.



ROSENBLUM, ALBERT F., Los Angeles. Died 9 August 1967 in Los Angeles of coronary artery disease, aged 66. Graduate of the University of Illinois College of Medicine, Chicago, 1928. Licensed in California in 1951. Doctor Rosenblum was a member of the Los Angeles County Medical Association.



TROTTER, ALFRED D., Los Angeles. Died 23 August 1967 in Los Angeles of carcinoma of the stomach, aged 68. Graduate of the University of Tennessee College of Medicine, Memphis, 1928. Licensed in California in 1930. Doctor Trotter was a member of the Los Angeles County Medical Association.



WEGROCKI, HENRY J., Los Angeles. Died 27 August 1967 in Duarte of Hodgkin's disease, aged 58. Graduate of the University of Minnesota Medical School, Minneapolis, 1940. Licensed in California in 1941. Doctor Wegrocki was a member of the Los Angeles County Medical Association.



WILLS, IRVING, Santa Barbara. Died 5 September 1967 in Santa Barbara, aged 73. Graduate of Rush Medical College, Chicago, Illinois, 1921. Licensed in California in 1923. Doctor Wills was a retired member of the Santa Barbara County Medical Society and the California Medical Association, and an associate member of the American Medical Association.



ZUNDEL, FREDERICK M., Oroville. Died 7 August 1967 at Lake Almanor, aged 54. Graduate of Northwestern University Medical School, Chicago, 1945. Licensed in California in 1948. Doctor Zundel was a member of the Butte-Glenn Medical Society.

PUBLIC HEALTH REPORT

Lester Breslow, M.D., M.P.H.
Director, State Department of Public Health

EARLIER THIS YEAR the State Department of Public Health was given authority to establish two regional centers for the treatment of chronic uremia. The centers, one in San Francisco General Hospital, and the other in Los Angeles County General Hospital, were established in accordance with Assembly Bill 2202.

Initially, dialysis services will be provided by each facility for 30 in-center patients, and there are plans to develop 20 units each for patients at home. The centers also will provide training for medical and nursing personnel who will carry out dialysis services in other parts of the state. A vital function of the facilities will be to work closely with other medical specialists to develop successful means of kidney transplantation.

Five patients currently are undergoing chronic hemodialysis at each center despite the fact the centers are still remodeling, purchasing equipment and recruiting and training personnel.

Only physicians licensed to practice medicine in California are authorized to refer patients. The initial contact is with the medical director, who advises the physician concerning the course of action he considers indicated.

If the patient is to be evaluated at the center, referral forms are provided and a date of evaluation set. Transportation costs to the center and costs for evaluation are borne by the patient, his family or by third party payments. Patients found medically suitable for chronic hemodialysis, on original evaluation, are then referred to a Patient Selection Committee composed of physicians, social workers, rehabilitation workers and other specialists as indicated.

The committee then considers the patient from an overall standpoint as to the feasibility of accepting him for the program. Upon selection, a plan of payment for services is arranged and chronic hemodialysis is initiated.

For patients considered suitable for home dialysis, it is necessary to train the patient and a member at the center for approximately two months.

When the point is reached that dialysis of the patient can be carried out in his home, it is then necessary to install equipment in the home and make all other arrangements to begin home dialysis immediately upon the patient's leaving the center. The staff at the center retains supervisory control over all patients in this program; and consultation and support, as required, are provided to the patient and his private physician.

Physicians desiring additional information or having patients for possible evaluation should contact:

Dr. Benjamin Barbour, Chief
Southern California Renal-Dialysis
Rehabilitation Center
Los Angeles County General Hospital
1200 North State Street
Los Angeles 90033

Dr. Frank Gotch, Director
Northern California Artificial Kidney Center
San Francisco General Hospital
22nd Street and Potrero Avenue
San Francisco 94110

* * *

As we come to the end of the 1967 measles epidemiologic season, it is appropriate to review the incidence statistics for this year as compared with similar periods in the past.

Since 1964, the reported number of cases has been declining steadily. The year 1964 was one of high incidence, 34,312 cases having been recorded. In 1965, there were 13,889 cases reported, a reduction which in part could be expected due to the normal cyclic incidence of the disease.

Based on the incidence of previous years, 1966 should have shown a relatively high number of cases had it followed the usual cyclic trend. There was, in fact, evidence of epidemic activity in several counties in the state. The number of reported cases, however, was only slightly higher (15,257) than that for 1965 and was less than half the

number in 1964. Prompt action in two counties to immunize large numbers of children apparently succeeded in aborting large scale epidemics. In addition, mass immunization campaigns were waged in several areas of California.

Despite epidemic activity in several counties this spring, the number of cases of measles reported thus far in the 1967 season indicates the lowest incidence since 1929 when the state's population was only about one-fifth what it is now. As

of 30 September this year, 4,987 cases have been reported, compared with 14,623 and 13,002 for the corresponding periods of 1966 and 1965 respectively.

Widespread use of measles vaccine by private physicians and health departments has undoubtedly played a major role in lowering incidence.

Measles need no longer occur. Increased use of measles vaccine can be expected to reduce the number of cases even further in the future.



NEWS & NOTES

NATIONAL • STATE • COUNTY

LOS ANGELES

The Twentieth Annual **Mid-Winter Radiological Conference**, sponsored by the Los Angeles Radiological Society, will meet at the International Hotel (adjacent to the Los Angeles Airport), Los Angeles, January 27 and 28, 1968.

The program will include the following speakers: Dr. Harold Jacobson, professor of radiology at Albert Einstein School of Medicine, New York City; Dr. Edward B. D. Neuhauser, director of radiology, Children's Medical Center, Boston; Dr. Gunner Vestby, Ulleval Hospital, Oslo, Norway; Dr. Thomas Lodge, United Sheffield Hospital, Sheffield, England; and Dr. Ralph M. Scott, professor of radiology (radiation therapy), University of Louisville School of Medicine, Louisville, Kentucky.

* * *

A one-day **conference on reading problems** will be sponsored by the Los Angeles Society of Ophthalmology in conjunction with the various colleges, universities, medical schools and boards of education of Los Angeles on Sunday, 21 January 1968, from 8:00 a.m. to 4:30 p.m., at the Statler Hilton Hotel. Representatives of the departments of education, neurology, ophthalmology, otolaryngology, psychiatry, psychology and sociology will participate in this program. Further information may be obtained from Los Angeles Society of Ophthalmology, Attention: Dr. George K. Kambara, 321 East 2nd Street, Los Angeles 90012.

* * *

A symposium on **recent advances in geriatrics** will be held 1 November 1967 at the Veterans Administration Hospital in Sepulveda. All inquiries concerning this conference should be directed to: Harry Sobel, Ph.D., Chief, Aging Research, VA Hospital, Sepulveda 91343.

Four recent **appointments to the faculty** of the University of California, Davis, School of Medicine, have been announced from the office of Dean C. J. Tupper:

Dr. Paul D. Hoepflich, who has been named professor of internal medicine, comes to Davis from the University of Utah College of Medicine, where he was associate professor of medicine and associate research professor of pathology.

Dr. Jerry P. Lewis, who is to be associate professor of internal medicine, comes from the faculty of the University of Illinois.

Dr. Makepeace U. Tsao (Ph.D.), associate professor of biochemistry at the University of Michigan, has been appointed professor of biochemistry in the Division of Surgical Science. Dr. Tsao taught in the Department of Pediatrics and Communicable Diseases at the University of Michigan from 1952 to May 1967. His extensive research has been primarily in such areas as experimental diabetes, potential anti-cancer compounds, human growth hormones and chemical causes of mental retardation.

Dr. Edwin S. Munson has joined the Davis faculty as assistant professor of anesthesiology. Dr. Munson, who held a similar academic rank at the University of Virginia School of Medicine at the time of his appointment, was an assistant professor at the University of California San Francisco Medical Center in 1964.

GENERAL

The Arizona Chapter of the **American College of Surgeons** will hold the annual meeting for 1968 at Del Webb's Townhouse in Phoenix, January 12 and 13, 1968. Further information may be obtained from Dr. James A. Laugharn, Maryvale Medical Center, 4550 North 51st Street, Phoenix, Arizona 85031.

* * *

The 12th annual meeting of the **Medical Society of the United States and Mexico** will be held at Guadalajara, Mexico, February 7-10, 1968. Further information may be obtained from Dr. James Nauman, 1603 North Tucson Boulevard, Tucson, Arizona 85716.

Rabies

Suggested Indications for Treatment of Exposed Persons

GEORGE L. HUMPHREY, D.V.M., M.P.H., *Berkeley*

THE RECOMMENDATIONS made here for the treatment of persons exposed to rabies have been prepared by the California State Department of Public Health and were endorsed by the California Conference of Local Health Officers 29 October 1966.

The recommendations are based on those of the World Health Organization Expert Committee on Rabies, Fifth Report,⁸⁰ with modification and addenda apropos the occurrence of the disease in California. The document constitutes a revision of the previous recommendations published by the Department in 1960¹⁷ and in a *Manual for the Control of Communicable Diseases in California*.²

The most important revisions incorporated in the present document concern: (1) local treatment of bite wounds, (2) information on the comparative efficacy of duck-embryo (D-E) rabies vaccine and nerve-tissue Semple type (N-T) vaccine, (3) pre-exposure immunization of man against rabies, and (4) up-dating of information on the disease in California.

From the Veterinary Public Health Section, Bureau of Communicable Diseases, California Department of Public Health.

Part of the Special Conference on Comparative Medicine Presented Jointly by the California Veterinary Medical Association and the Scientific Board of the California Medical Association at the 96th Annual Session of the California Medical Association, Los Angeles, April 15 to 19, 1967.

Reprint requests to: Veterinary Public Health Section, Bureau of Communicable Diseases, California Department of Public Health, 2151 Berkeley Way, Berkeley 94704.

Recent experimental trials in animals have strongly indicated that prompt and adequate local treatment of bite wounds is of primary importance in preventing rabies infection, and presumably this would apply also to humans. The work done on local wound treatment strongly suggests that certain agents be used and, more important, that a precise method be followed in using them.

The rationale suggested by current knowledge is to:

1. Swab and flush the bite wound vigorously and repeatedly with either soap or quarternary ammonium solution* (preferably benzalkonium chloride).

2. Apply topically to the wound hyperimmune antirabies serum (optional in instances of mild exposure, recommended for severe exposure).

3. Infiltrate under the wound itself with hyperimmune antirabies serum (hereinafter referred to simply as antirabies serum) where feasible to do so in all instances of severe exposure.

4. Administer the recommended systemic antirabic treatment, using either rabies vaccine alone for mild exposure or combined antirabies serum and vaccine for severe exposure (See *Outline Guide of Suggested Treatment*, Table 4.)

*Soap and the quarternary ammonium compounds are chemically incompatible.

The systemic use of antirabies serum is reserved for instances of severe exposure (multiple bites; face, head, finger or neck bites; or bites by certain wild species), due to the frequent occurrence of delayed serum sickness type reactions.

TABLE 1.—*Known Infectious (Virus in Saliva) Periods for Rabies in Various Animal Species*

| Species | Maximum Periods that Rabies Virus Has Been Isolated from Saliva or Salivary Glands | |
|----------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|
| | Before Onset of Overt Disease*† | Before Death‡ |
| Dog | 5 days ^{35,68} | 12 days ^{36,68} |
| Cat | 1 day ⁷⁰ | 6 days ⁷⁰ |
| Skunk | 5 days ⁶⁴ | 18 days ⁵¹ |
| Fox | 3 days ^{64,68} | 17 days ^{42,66,68} |
| Bats (Insectivorous) | Some individuals may be in the early stages of the disease. Data of the type obtained for the carnivores are not available for bats ^{13,66,68,69} | |
| Other Species | Information not available | |

*Classic signs of rabies or paralysis. Prodromal signs such as fever, irritability and various types of abnormal behavior will be present preceding the onset of overt signs of clinical illness. During the early stages of the disease, abnormal behavior may not be constantly present but be exhibited in cycles.³⁶

†Reference numbers quoted refer to those listed at the end of the paper.

Both N-T† and D-E‡ type rabies vaccines are commercially available in the United States. The N-T product may occasionally cause neurologic complications, D-E vaccine less frequently. Duck-embryo rabies vaccine is the type now most commonly used in the United States but is clearly less potent than N-T vaccine.

Duck-embryo vaccine is the present product of choice for pre-exposure immunization of persons at high risk of exposure but N-T vaccine is probably the best choice for post-exposure treatment, particularly when combined antirabies serum and rabies vaccine are administered to severely exposed persons.

The attending physician must exercise judgment which will logically result in variation in therapeutic procedure for individual patients based on the circumstances under which exposure occurs and the clinical status of the patient. The variable factors with reference to authoritative knowledge and the circumstances surrounding a particular situation

†National Drug Company, Philadelphia.
‡Eli Lilly and Company, Indianapolis.

TABLE 2a. — *Frequency of Positive Results for Rabies by Species in Animals Examined by the California Department of Public Health, 1950-1963*

| Species | Examined | Positive for Rabies* | | Species | Examined | Positive for Rabies* | |
|-----------------------|----------|----------------------|-----------|-----------------------|----------|----------------------|-----------|
| | | No.‡ | Per Cent† | | | No.‡ | Per Cent† |
| Skunk | 1,988 | 1,028 | 51.7 | Weasel | 89 | | |
| Bovine | 373 | 101 | 27.1 | Deer | 26 | | |
| Badger | 10 | 2 | 20.0 | Chinchilla | 13 | | |
| Bobcat | 62 | 12 | 19.4 | Mink | 12 | | |
| Equine | 96 | 14 | 14.6 | Vole | 9 | | |
| Fox | 598 | 83 | 13.9 | Hawke | 9 | | |
| Bat | 1,071 | 138 | 12.9 | Pig ^d | 8 | | |
| Goat | 9 | 1 | 11.1 | Ocelot | 8 | | |
| Coyote | 93 | 7 | 7.5 | Bear | 7 | | |
| Sheep | 19 | 1 | 5.3 | Owl ^e | 6 | | |
| Dog | 6,054 | 232 | 3.8 | Porcupine | 5 | | |
| Raccoon | 285 | 7 | 2.5 | Mountain lion | 3 | | |
| Monkey | 153 | 2 | 1.3 | Gibbons ape | 3 | | |
| Cat ^a | 4,730 | 24 | 0.5 | Prairie dog | 3 | | |
| Gopher | 1,412 | | | Beaver | 2 | | |
| Squirrel ^b | 1,358 | | | Coatimundi | 2 | | |
| Rat | 1,090 | | | Chicken ^e | 2 | | |
| Mouse ^c | 942 | | | Ferret | 1 | | |
| Hamster | 639 | | | Wolf | 1 | | |
| Rabbit ^d | 319 | | | Nutria | 1 | | |
| Chipmunk | 262 | | | Tapir | 1 | | |
| Muskrat | 129 | | | Kinkajou | 1 | | |
| Opossum | 128 | | | Pheasant ^e | 1 | | |
| Guinea pig | 113 | | | Parakeet ^e | 1 | | |
| Mole | 92 | | | Unknown ^g | 130 | 1 | |
| TOTALS | | 22,369 | 1,653 | | | 7.4 | |

*Positive for rabies by microscopic examination for Negri bodies, mouse inoculation or fluorescent rabies antibody (FRA).

†Percentage calculated to nearest one-tenth per cent.

‡Of the total of 1131 specimens reported positive during the 11-year period, 1950-1960, 627 were positive by mouse inoculation.

^a—Includes both domestic and feral house cats.

^b—Includes both tree and ground squirrels.

^c—Includes field and house mice and pet white mice.

^d—Includes both domestic and wild rabbits.

^e—Avian species are not considered to play any role in rabies.

^f—One hog reported positive for rabies by the Los Angeles County Health Department in 1956.

^g—Species not stated or unknown.

SOURCE: State of California Department of Public Health Laboratory Report Records.

can be expected to influence the pattern of prophylaxis to be followed. The recommendations made here have been prepared with a view to providing information which will be of assistance to persons involved with decision for the administration of human antirabic treatment in California. The date of final preparation of these recommendations is October 1966.

The Decision to Treat

Utilization of Veterinary Clinical Judgment. The first problem arising in any medical situation concerning rabies is basically a veterinary one—that is, determination of the health status of the biting animal. This question is important in that specific antirabic treatment of the bitten person is not necessary if the exposure has not involved rabies virus.³⁰ In many instances, decision to administer treatment will depend upon the health status of a biting animal which is available for observation. The use of veterinary clinical judgment as to the health status of a biting animal can often be helpful in deciding the need for initiating systemic antirabic treatment.

It is seldom necessary to initiate systemic treatment as long as the biting animal remains normal (an exception is bats, for sometimes apparently normal bats may be in the early stages of the disease). Where decision to initiate treatment of a bitten person may hinge upon determination of the health status of an available suspect animal, the services of a veterinarian should be used if available. Under California law, only a veterinarian is legally qualified to render clinical judgment of rabies infection in animals.

The Infectious Period. In determining the need for systemic antirabic treatment of a bitten person, the period of time during which rabies virus may be present in the saliva of a rabid animal is important, in particular that period preceding the onset of frank overt signs of a disease—classical signs of rabies or paralysis.

Rabies virus invades the salivary glands and may be present in the saliva of a variable proportion of naturally infected animals. In most infected animals, rabies virus does not occur in the saliva until after the onset of frank clinical signs of the disease; in a few the occurrence of virus in the saliva will precede overt clinical signs by a variable period.

It is almost impossible to define any overt sign or symptom in the pathogenesis of the disease other than paralysis or death for use as a "landmark" in

saying that rabies virus would not have been present in the saliva more than a specified number of days before the landmark appeared.

It is doubtful, however, that rabies virus will be present in the saliva of an infected animal before the initial onset of fever.³⁶ In addition, one or more prodromal signs such as hyperactivity, irritability, change in disposition, diminution of corneal reflex, abnormal appetite (eating of wood, dirt, stones, feces, bedding, etc.) will be apparent to an informed observer. Early in the clinical course of infection, such subjective signs as abnormal behavior or activity are not always constantly present but may occur in increasingly frequent cycles as the disease progresses.

In rabid wild animals—skunks, foxes, coyotes, racoons, bobcats and weasels, for example—such abnormal behavior as daytime appearance, loss of fear of humans and human habitation or attacks upon man, domestic pets or livestock, all carry an extremely high order of suspicion of rabies. Also, taking young wild animals found abroad during daytime in areas where rabies exists in wildlife may result in exposure to rabies. The very young of any species are extremely susceptible to rabies. Rabid mother skunks, for example, may infect their entire litter before dying of the disease. In young skunks thus infected rabies may not develop until several months later, long after they may have been taken into the home as pets. An incubation period as long as 177 days has been reported in skunks.³¹

The information available on the infectious period for rabies in different species is included in Table 1. The information in this table can be useful from the standpoint that if a biting animal, a cat for example, remains healthy (without fever or signs of abnormal behavior) for two or more days after it has bitten someone, one may presume that the cat was not infectious at the time of biting.

Relative Risk of Rabies Infection. In weighing the question of systemic antirabic treatment of a person bitten by an animal or otherwise exposed, consideration should be given to the risk of incurring serious reaction to treatment as against the risk of incurring rabies. The risk associated with antirabic treatment is fairly well known and reaction rates have been reported by various authorities (see section on Systemic Antirabic Treatment, page 370). On the other hand, the risk of incurring rabies infection from a particular exposure often-times cannot be so well established.

Certain data are available, however—for exam-

ple, the relative frequency of positive findings for rabies in various species of animals examined in California—which permit some degree of evaluation as to the relative risk of exposure to rabies infection from various species of animals. Certain species have never been found rabid despite numerous laboratory examinations extending over many years. The data available provide a basis of experience as to the relative frequency of positive findings in laboratory examinations, by species, in animals examined by the State Department of Public Health during the 14-year period 1950-1963 (Table 2a) and in California as a whole during 1964-1965 (Table 2b).

High Risk Species. Bites inflicted by such species as the striped skunk, spotted skunk (civet or "Phobey cat"), bobcat, fox, badger, bat and coyote (in descending order of risk), should be considered to carry a relatively high risk of exposure to rabies unless proved otherwise.

Bites from such species as the dog, racoon and cat carry a lesser degree of risk (less than five per cent of biting animals submitted for examination found positive) than the preceding group of animals (Tables 2a and b).

Exposure to cattle—as, for example, in administration of medication or the like to an ill animal which later comes under suspicion of being rabid—also carries a high risk (27 per cent of such animals submitted for examination were found rabid. See Table 2a).

Low Risk Species. Bites inflicted by such species as gophers, various squirrels, wild rats, pet white rats, wild mice, pet white mice, hamsters, wild and domestic rabbits, chipmunks, muskrats, opossums, guinea pigs, moles and chinchillas and others, are considered to carry an extremely low order of risk of rabies infection⁵⁴ and seldom if ever should necessitate systemic antirabic treatment of the bitten person (Tables 2a and b).

Pet white rats and white mice, hamsters, domestic rabbits, pet chipmunks and squirrels, guinea pigs, etc., can be further evaluated from the standpoint of where these pets have been kept and what animals they have had contact with in the period preceding infliction of the bite. In the absence of contact with a rabid animal—and such contact is extremely unlikely in the environment that such pets are usually kept—the possibility of rabies can often be excluded on the basis of the history of the animal involved.

Current Situation. In evaluating the degree of

TABLE 2b. — *Frequency of Positive Examinations for Rabies by Species in Animals Examined in California, 1964-1965*
(Consolidated State and Local Examinations)

| Species | Examined | Positive for Rabies* | |
|--------------------------|----------|----------------------|----------|
| | | Number | Per Cent |
| Skunk† | 1,118 | 323 | 28.9 |
| Equine | 31 | 8 | 22.6 |
| Bovine | 98 | 23 | 23.6 |
| Bobcat | 28 | 3 | 10.7 |
| Bat | 1,118 | 117 | 10.5 |
| Badger | 12 | 1 | 8.3 |
| Fox | 277 | 14 | 5.1 |
| Coyote | 42 | 2 | 4.8 |
| Dog | 2,976 | 65 | 2.2 |
| Opossum | 99 | 1 | 1.0 |
| Racoon | 146 | 1 | 0.7 |
| Cat | 4,097 | 3 | 0.1 |
| Gopher | 1,679 | | |
| Hamster | 1,515 | | |
| Mouse‡ | 1,280 | | |
| Rat§ | 900 | | |
| Squirrel | | | |
| Ground | 572 | | |
| Tree | 100 | | |
| Kind not stated | 169 | | |
| Rabbit | 346 | | |
| Guinea pig | 231 | | |
| Chipmunk | 198 | | |
| Monkey | 135 | | |
| Weasel | 81 | | |
| Muskrat | 65 | | |
| Mole | 64 | | |
| Rodent, kind not stated | 17 | | |
| Ocelot | 12 | | |
| Sheep | 9 | | |
| Deer | 9 | | |
| Mink | 9 | | |
| Seal | 8 | | |
| Pig | 6 | | |
| Goat | 5 | | |
| Leopard | 3 | | |
| Owl | 3 | | |
| Species not listed above | 30 | | |
| TOTALS | 17,488 | 560 | 3.2 |

*Positive for rabies by microscopic examination for Negri bodies, mouse inoculation or fluorescent rabies antibody (FRA).

†Skunk (including spotted skunk).

‡Mouse (including house and field mouse and vole).

§Rat (including kangaroo rat).

SOURCE: State of California, Department of Public Health, Laboratory Records.

TABLE 3. — *Frequency of Negri Positive Specimens by Species in Rabid Animals Examined by the California State Department of Public Health, 1950-1960*

| Species | Confirmed by Mouse Inoculation | With Negri Bodies | |
|---------|-----------------------------------|-------------------|----------|
| | | Number | Per Cent |
| Skunk | 343 | 187 | 55 |
| Dog | 110 | 32 | 29 |
| Fox | 55 | 14 | 25 |
| Bovine | 54 | 11 | 20 |
| Bat | 30 | 5 | 17 |
| Cat | 13 | 2 | 15 |
| Bobcat | 8 | 1 | 13 |
| Equine | 6 | | 0 |
| Racoon | 5 | 1 | 20 |
| Goat | 1 | | |
| Sheep | 1 | | |
| TOTAL | 626 | 253 | 41 |

SOURCE: State of California Department of Public Health, Laboratory Records.

TABLE 4.—Outline Guide of Suggested Treatment of Persons Exposed to Rabies, California State Department of Public Health, 1966

A. LOCAL TREATMENT

1. First-aid Treatment

Immediate washing and flushing with copious soap and water, detergent and water or water alone as soon as possible. (Warning: See footnote a.)

2. Treatment by a Physician

- Thorough cleansing by vigorous swabbing and flushing with 20 per cent green soap solution or 0.1 per cent (1:1000) or 1.0 per cent (1:100) quarternary ammonium compound. (Warning: See footnotes a and b.)
- Topical application of hyperimmune antirabies serum by vigorous swabbing and flushing (optional in instances of mild exposure but definitely recommended in all instances of severe exposure).
- Immediate suturing of the wounds is not recommended.
- Infiltration of hyperimmune antirabies serum around and under the wound where feasible is recommended in all instances of severe exposure.

B. SPECIFIC SYSTEMIC TREATMENT

| Nature of Exposure | Health Status of Biting Animal | | Suggested Systemic Treatment (rabies vaccine, antirabies serum) |
|------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| | At Time of Exposure | During Observ. Period of 10 Days | |
| I. No lesion; indirect contact only | Rabid | | None |
| II. Licks of: | | | |
| (1) Unabraded skin | Rabid | | None |
| (2) Abraded skin, scratches and unabraded or abraded mucosa | (a) Healthy (b) Healthy (c) Signs suggestive of rabies (d) Rabid, escaped, killed or unknown | Healthy Clinical signs of rabies or proved rabid (laboratory) Healthy | None Start vaccine at first signs of rabies in the biting animal. ^c Start vac. immed.; stop treatment if animal is normal on 5th day after exposure. Start vaccine immediately. ^c |
| III. Bites: | | | |
| (1) Mild exposure (other than multiple bites or face, head, finger or neck bites). | (a) Healthy (b) Healthy (c) Signs suggestive of rabies (d) Rabid, escaped, killed or unknown (e) Wild (skunk, bobcat, fox, bat, etc.) | Healthy Clinical signs of rabies or proved rabid (laboratory) Healthy | None Start vaccine at first signs of rabies in the biting animal. ^c Start vac. immed.; stop treatment if animal is normal on 5th day after exposure. Start vaccine immediately. ^c Serum immediately, followed by vaccine. ^d |
| (2) Severe exposure (multiple bites or face, head, finger or neck bites). | (a) Healthy (b) Healthy (c) Signs suggestive of rabies (d) Rabid, escaped, killed or unknown (e) Wild (skunk, bobcat, fox, bat, etc.) | Healthy Clinical signs of rabies or proved rabid (laboratory) Healthy | Serum immed.; no vac. as long as animal remains normal. Serum immediately, start vaccine ^d at first sign of rabies in the biting animal. Serum immediately, followed by vaccine. Vaccine may be stopped if animal is normal on 5th day after exposure. Serum immediately, followed by vaccine. ^d Serum immediately, followed by vaccine. ^d |

a—Where soap has been used, all traces of it should be removed before application of quarternary ammonium compounds because the latter are neutralized by soap.

b—Quarternary ammonium compounds: (1) ZEPHIRAN—Winthrop Laboratories, New York, N. Y.—high molecular alkyl-dimethyl benzalkonium chloride. Available as a 17 per cent buffered aqueous stock solution and diluted 1:17 in distilled water to yield a 1.0 per cent (1:100) concentration and 1:170 for a 0.1 per cent (1:1000) concentration for bite wound treatment. (2) PHEMEROL—Parke Davis and Co., Detroit, Mich.—high molecular alkylamine hydrochloride (benzethonium chloride). Available as a 5.0 per cent aqueous stock solution containing added amber dye to mark the area of topical application. It should be noted that in a 1.0 per cent concentration, the quarternary ammonium compounds will have some deleterious effect on tissues. Care should be exercised to avoid retention in puncture wounds. A concentration of 0.1 per cent while less effective in experimental rabies prevention should have no deleterious effect on tissues. The 1.0 and 0.1 per cent concentrations should not be used on mucous membranes or near the eyes.

c—The course of rabies vaccine should consist of a minimum of 14 doses (one per day) followed by booster injections at 10 and 20 days following the last dose. Booster injections are especially indicated where combined hyperimmune antirabies serum and vaccine have been used.

d—In all cases of severe exposure and in all cases of unprovoked bites by wild animals, e.g., skunks, bats, foxes, bobcats, racoons in California, hyperimmune antirabies serum together with 14 doses of vaccine and booster injections at 10 and 20 days following the 14 dose course should be given.

NOTE: This table is similar to but differs in minor respects from the guide contained in the WHO Expert Committee on Rabies, Fifth Report, World Health Organization, Technical Report Series, No. 321, 1966, pp. 34-35.

risk associated with a particular exposure, it should be kept in mind that the relative frequency of rabies infection in animals examined for rabies originating from a specific area may vary widely from far below to far above the composite percentages shown in Tables 2a and b. Local health officers, however, can supply specific information on the current rabies situation within their respective areas and should be consulted in this connection.

Saliva Contact

Unabraded Skin. The exposure of intact skin to saliva of a rabid animal should not warrant systemic antirabic treatment. All available evidence supports the concept that infection is dependent upon the implantation of an infective dose of rabies virus in or near nerve tissue.

Abraded Skin or Scratches. Systemic antirabic treatment should be considered a necessity if abraded skin or scratches without eschar or less than 24 hours old are contaminated with saliva of a rabid animal. If the abrasions or scratches do have eschar or are more than 24 hours old, the contamination may be considered as contamination of intact skin, and not necessitating system antirabic treatment.^{60,80}

Abrasions or Scratches Inflicted by Claws. Abrasions or scratches of skin inflicted by the claws of an animal suspected of rabies should be considered as a possible exposure to infection. At times, such injuries may be quite severe. The possibility of exposure to rabies arises because if an animal were rabid and virus were present in the saliva, the claws might have been contaminated by the animal licking them just before inflicting the abrasions or scratches. Hence, decisions regarding systemic antirabic treatment of a person incurring injuries inflicted by the claws of a cat should be guided by the same considerations as for bite injuries, that is, the degree and location of the wounds and the health status of the cat at the time of inflicting the injury and during the period of observation afterward.

Severity of Exposure. Bite wounds inflicted on the head, face and neck regions and fingers and multiple bites in other areas carry an increased risk of rabies infection. The transmission of rabies is dependent upon the implantation of an infective dose of virus in or near nerve tissue. The more dense concentration of sensory nerve endings in the head, face, neck and finger regions probably accounts for the greater risk of infection observed with exposure in these areas. Similarly, the more

extensive the bite wounds inflicted, the greater the risk of infection due to the greater chance of exposing nerve tissue to an infective dose of rabies virus. Such exposures are considered severe and warrant the best treatment available — adequate local treatment, infiltration of antirabies serum under the wound, systemic administration of antirabies serum and a full 14-dose course of rabies vaccine with two booster injections as outlined hereinafter.

Local Antirabic Treatment of Bite Wounds

The primary importance of early adequate local treatment of bite wounds was stated in the previously mentioned 1960 recommendations for antirabic treatment.^{2,17} However, recent experiments in animals^{20,39,53,76} have explored new approaches to local treatment, the effectiveness of which recommend the use of certain agents and suggest that a certain method be followed in using them.

It has been shown that rabies virus inoculated intramuscularly in animals can persist at the site of inoculation for 24 hours and in some instances up to 72 to 96 hours.^{29,43,58} However, the virus level drops sharply following injection.⁵⁸ The objective of local treatment of bite wounds is to reduce the amount of rabies virus implanted in the wound to below the infective dose level. The level of virus may be reduced through dilution (swabbing and flushing), virucidal action of the agent used or a combination of both.

Experiments in animals have demonstrated such agents as tap water and soap, 20 per cent green soap solution, quarternary ammonium compound,*† nitric acid or antirabies serum to be effective in preventing rabies when used locally at the site of exposure. Soap, quarternary ammonium compound, nitric acid and antirabies serum all possess virucidal ability. Nitric acid is corrosive and will produce a high degree of local tissue reaction as compared with either soap or antirabies serum. Benzalkonium chloride in 1.0 per cent concentration has been shown to be effective in the local treatment of wounds in guinea pigs infected with

*Soap and the quarternary ammonium compounds are chemically incompatible.

†Quarternary ammonium compounds:

(1) High molecular alkyl-dimethyl benzalkonium chloride, ZEPHRAN®—Winthrop Laboratories, New York, N.Y. Available as a 17 per cent buffered aqueous stock solution. The 17 per cent stock solution is diluted 1:17 to yield a 1.0 per cent (1:100) concentration and 1:170 for a 0.1 per cent (1:1000) concentration for bite wound treatment. See discussion above regarding corrosive nature of 1.0 per cent solution upon tissue.

(2) High molecular alklamine hydrochloride (benzethonium chloride), PHEMEROL®—Parke Davis and Co., Detroit, Michigan. Available as a 3.0 per cent aqueous stock solution containing added amber dye to mark the area of application.

rabies virus, but in a 1.0 per cent concentration benzalkonium chloride will also have a deleterious effect upon tissues.⁸⁰ Shaughnessy and Zichis,⁶³ however, report that 1.0 per cent benzalkonium chloride did not cause burns or scarring or interfere with wound healing.* The 0.1 and 1.0 per cent concentrations of the quarternary ammonium compounds should not be used on mucous membranes or about the eyes, however. The fact that 1.0 per cent benzalkonium chloride has proved more efficacious than a concentration of 0.1 per cent or than 20 per cent soap solution would recommend the use of 1.0 per cent benzalkonium chloride as the agent of choice for local treatment of bite wounds.

The literature cited include local treatment of superficial wounds but some is primarily concerned with the local treatment of deep puncture wounds which are difficult to treat satisfactorily.^{20,39}

First Aid Treatment. The effectiveness of such simple and widely available agents as tap water and soap in preventing rabies in experimental animals with superficial non-puncture wounds suggests that such treatment should be applied when other agents are not available or there is delay in reaching a physician.²⁰ Often exposures are scratches and minor lacerations or bites. In such cases, first aid treatment using soap and water pending more adequate care by a physician will materially reduce the risk of rabies infection.

Superficial Wound Treatment. Agents effective experimentally in antirabic treatment of superficial wounds in animals were tap water, Ivory soap and water, Ivory soap and water followed by topically applied antirabies serum, 20 per cent green soap solution, and 1.0 per cent aqueous benzalkonium chloride.²⁰ All the foregoing agents provided significant protection when applied within three hours after exposure by vigorous scrubbing and flushing of the wounds, using cotton pledgets.²⁰

Treatment of Puncture Wounds

Swabbing and Flushing. Repeated swabbing and flushing with 20 per cent green soap solution,³⁹ aqueous benzalkonium chloride,^{20,39} antirabies serum²⁰ or combinations thereof²⁰ in deep puncture wounds reduced the degree of infection (but here again the warning that soap and the quarternary ammonium compounds are chemically incompatible. Hence, any residual traces of either should be

flushed away before the other is used).

The method of treatment suggested by recent investigations^{20,39} is that repeated vigorous swabbing (twirling) of the wound depths should be carried out, using six tightly twisted cotton-tipped applicators twirled four times each after they have been dipped in the agent being used, combined with deep flushing by use of a blunted hypodermic needle attached to a 5 to 20 ml syringe inserted into the depths of the wound. It should be emphasized that the above method of application is more important than the nature of the agent used.³⁹ In experimental animal trials with less vigorous methods of treatment, the mortality rate was higher.^{20,39}

Vigorous swabbing and flushing with benzalkonium chloride within 12 hours after exposure, and with serum within six hours, gave significant protection.²⁰ Similar treatment using 20 per cent green soap solution within one hour provided significant protection.³⁹

Swabbing and flushing with antirabies serum is optional in instances of mild exposure and is recommended in all instances of severe exposure.

Possible sensitivity to antirabies serum should be determined in all instances before topical use is made of serum (see section on Systemic Antirabic Treatment).

Infiltration of Antirabies Serum Under Wound. There is sufficient experimental evidence to show that infiltration of antirabies serum under the wound itself is effective in preventing rabies infection in animals.^{20,39,40,53} Presumably this is true also in humans, although clinical evidence on this point is lacking. The dose of serum used for local infiltration will be dictated chiefly by the site of the bite wound. However, where possible, not less than 5 ml is recommended. Sensitivity to antirabies serum should be determined before it is used (see section on Systemic Antirabic Treatment). Infiltration under the wound is recommended in all instances of severe exposure.⁸⁰

Nitric Acid. The specific value of nitric acid applied locally to bite wounds is clear. There is no evidence that nitric acid is more effective than 1.0 per cent benzalkonium chloride or 20 per cent green soap solution.⁸⁰ Moreover, the use of nitric acid is probably more subject to variables in method or degree of treatment in the course of normal medical practice than would be the use of 1.0 per cent benzalkonium chloride or green soap solution. This fact as well as the caustic nature of nitric acid suggests limited use of this chemical in

* Care should be exerted to flush residual traces of the drugs in such concentrations from the depths of puncture wounds.

local wound therapy for the prevention of rabies.^{39,53,62,63}

Suturing of Bite Wounds. It is recommended that bite wounds not be immediately sutured, in light of evidence that early closure can be a contributing factor to the development of rabies infection.^{11,80}

Antiseptics and Antibiotics. The application of ordinary antiseptics and the local use of antibiotics, while they have no prophylactic value against rabies, may follow local treatment to combat bacterial infection.⁸⁰ However, the thorough cleansing and debridement recommended for bite wounds would suggest that antibiotics should not be necessary as a routine procedure.

Systemic Antirabic Treatment

Relative Efficacy of Various Treatment Regimens. Systemic antirabic treatment is based upon the administration of rabies vaccine alone or vaccine in combination with intramuscular injection of antirabies serum. It is generally conceded that combined serum and rabies vaccine provides the best protection in post-exposure treatment.⁸⁰ In descending order of efficacy: (a) combined serum and vaccine, (b) vaccine alone and (c) serum alone are the available methods of systemic post-exposure treatment.

The general principles upon which the *Outline Guide of Suggested Indications for Treatment* is based is that with mild exposures a course of rabies vaccine following the recommended local treatment is sufficient, whereas with severe exposure the combined use of antirabies serum and rabies vaccine should be employed.⁸⁰

Rabies vaccine should be administered in all instances as a course of 14 doses (one dose daily) plus booster injections of vaccine at 10 and 20 days after completion of the basic 14 dose course. Booster injections at 10 and 20 days following the basic course are particularly important when antirabies serum has been administered, due to interference of antirabies serum with the immune response to rabies vaccine.⁸⁰

Systemic Use of Antirabies Serum. While the use of rabies serum alone apparently exerts some saving effect, experimental results indicate that the chief effect of systemically administered serum is a definite prolongation of the incubation period.^{44,72,73} The greatest use for the serum is in conjunction with rabies vaccine for cases of severe exposure to rabies, in which the incubation period

is most likely to be very short.

Time Limit on Use. Experimental results in animals clearly indicate that the sooner antirabies serum is administered after exposure the better.^{58,77} The effectiveness in animals decreases rapidly when serum is administered more than 72 hours after exposure.^{44,72,77} While early use of antirabies serum is recommended, there is no time limit beyond which administration of serum is contra-indicated.⁸⁰ When antirabies serum is combined with rabies vaccine treatment, however, certain recommendations relative to administration should be noted due to an interference phenomenon on the part of antirabies serum with antibody response to the course of vaccine^{9,80} (see following paragraph).

Administration of Combined Antirabies Serum and Rabies Vaccine. If passive (serum) antibodies are maintained for too long a period by repeated systemic doses of antirabies serum or if less than a complete course of vaccine (14 doses plus booster injections at 10 and 20 days) is given after the single intramuscular dose of antirabies serum recommended, there occurs a definite interference phenomenon on the part of passive serum antibodies with the antigenic response to rabies vaccine as measured by neutralizing antibody titer.* In animals this interference phenomenon has also been confirmed by subsequent virus challenge.^{31,78} Doses of rabies vaccine given toward the end of the series, that is, after the 10th day, together with booster injections at 10 and 20 days following completion of the basic course, are active in overcoming such interference.^{31,80}

Recommendations for the combined use of antirabies serum and rabies vaccine, therefore, are that only a single administration of serum be given (minimum dosage, 40 international units (IU) per kilogram of body weight inoculated intramuscularly in the buttocks) followed by a course of 14 doses (one dose daily) of vaccine plus booster injections of vaccine at 10 and 20 days following completion of the basic 14-dose course.⁸⁰ Vaccine can be started at the time of administration of antirabies serum. The two booster inoculations of rabies vaccine are essential if the interference phenomenon is to be overcome. Antibody response to booster doses of rabies vaccine has been observed within three days following injection.⁸⁰

Reactions to Antirabies Serum and Sensitivity Testing. Reactions to antirabies serum, even though

* Reference Nos. 8, 9, 10, 78, 80.

concentrated and purified, occur approximately to the same degree as with other sera of equine origin. Reactions can be of the immediate anaphylactic type or the delayed serum sickness type. Serum sickness occurs in about 15 to 25 per cent of persons given serum of equine origin.⁸⁰ The incidence is less in children below 15 years of age.⁸⁰

An immediate reaction of anaphylactic type to antirabies serum can usually be avoided by the routine use of an intradermal or ophthalmic test for sensitivity.⁸⁰ Skin tests should not be administered unless a syringe containing one ml of 1:1000 epinephrine is available for immediate use.¹⁹ In the event of a positive reaction to a sensitivity test, the usual precautions of desensitization should be followed in administration of the serum.⁸⁰

While skin or ophthalmic tests are useful in anticipating possible anaphylactic type reactions, a negative test result does not preclude the presence of sensitivity and the subsequent development of delayed serum sickness reaction. Such reactions may have onset as much as 12 days⁶⁸ after administration of serum. The incidence and severity of reactions to antirabies serum can be reduced by the administration of an antihistamine drug.⁸⁰ It is recommended that an antihistamine be given daily for 10 to 12 days following administration of serum.

Treatment of Reactions to Antirabies Serum

1. *Epinephrine*. One ml of 1:1000 epinephrine should be available for immediate use in carrying out sensitivity tests or in topical or systemic administration of antirabies serum as a safeguard in the event of reaction of anaphylactic type.¹⁹

2. *Antihistamines*. The administration of an antihistamine for 10 to 12 days after injection of serum can reduce the incidence of serum sickness following the use of antirabies serum.

3. *Cortisone and Corticotropin (ACTH)*. These agents are extremely effective in controlling reactions to serum (serum sickness)¹⁴ and the neuro-paralytic reactions associated with the use of nerve-tissue Semple type vaccine.^{12,25,37,49} Although the foregoing products are effective in controlling reactions, evidence exists that they interfere with the development of active immunity elicited by vaccine¹⁴ and may possibly reactivate rabies infection in an exposed individual.⁶⁵

Experimental work in rabbits suggests that corticotropin (ACTH) may interfere less with production of active neutralizing antibody than does cortisone.¹⁴ However, neither product appears to

affect adversely the persistence of passive immunity induced through administration of antirabies serum.¹⁴ In instances of severe reaction, use of these agents should not be rigidly withheld, but they should be avoided if possible.

Post-Exposure Rabies Vaccine Treatment

Types of Vaccine Available. Semple type nerve-tissue (N-T) and duck-embryo (D-E) vaccine are the two types of human antirabic vaccine commercially available in the United States.

While the efficacy of human post-exposure antirabic treatment with vaccine is difficult to document, that treatment using various types of rabies vaccine does have a saving effect is generally accepted, based upon observation of extensive use throughout the world since vaccine was first administered by Pasteur 80 years ago.

In a group of 465 persons bitten in India by rabid animals which were proved capable of transmitting the virus (one or more of the persons or animals bitten died of rabies), 316 persons were given a complete series of treatment using Semple type nerve-tissue rabies vaccine and 106 persons received no treatment. In the treated group, 28 or 8.9 per cent died of rabies whereas 51 or 48.1 per cent of the untreated group died of the disease.⁷¹ Twenty-nine of the group of 465 persons cited above did not receive complete courses of Semple vaccine treatment, five or 17.2 per cent of whom died of rabies; and 14 other persons who died during the course of vaccine treatment are excluded from the relative mortality figures quoted for the completely treated and untreated groups.

Actively induced serum neutralizing antibodies resulting from daily inoculations of rabies vaccine are not detectable in many persons, however, until the tenth to the fifteenth day.^{10,23} In severely exposed persons, that is, those in which the incubation period is likely to be very short, antirabies serum should be used in combination with vaccine treatment,⁸⁰ as previously described.

Comparative Efficacy of Nerve-Tissue and Duck-Embryo Rabies Vaccines

The D-E product is the most commonly used of the two types of rabies vaccines now available, probably well in excess of 60 per cent of the total amount of vaccine used in California during recent years.¹⁵ The D-E vaccine has been commercially available since early in 1957.

Following its introduction, the California Department of Public Health was asked by local health officers to comment upon the efficacy of

D-E vaccine as compared with N-T vaccine. While recognizing that D-E vaccine probably carried less risk of neuroparalytic accident than did N-T vaccine, the Department felt that the question of efficacy of the D-E product as compared with N-T vaccine could not be answered with the information then available. Adequate data for making such a comparison still was lacking in 1960 when the previously mentioned recommendations for antirabic treatment were published.^{2,17} Experimental work carried out since 1961, however has shown that D-E vaccine is clearly less potent than N-T vaccine.^{21,74}

In tests conducted in the New York State Department of Health Laboratories,²¹ 13 (72.2 per cent) of 18 lots of commercial D-E rabies vaccine obtained on the open market in 1961 did not meet minimal Habel-test standards; the other five lots passed marginally. Six lots of D-E vaccine evaluated for potency by the National Institutes of Health (NIH) method failed to meet minimal standards established by the NIH for vaccines containing inactivated virus. The results of the foregoing work with D-E vaccine provided the impetus behind a 10-fold increase in duck-embryo tissue concentration made in the commercial product in 1962.²¹

In another report, post-infection treatment of guinea pigs with D-E vaccine in a dosage corresponding to that recommended for human treatment was shown to give very poor results whether the vaccine was used alone or in combination with antirabies serum.⁷⁴ Even when the dosage of D-E rabies vaccine was raised to the same level as that recommended for pooled Semple type N-T rabies vaccine, the results obtained with D-E vaccine given alone or in combination with different doses of serum were inferior to those obtained with N-T vaccine given under identical conditions. The investigators concluded from the results of their work that, on the basis of relative weights of the experimental animals and humans, the dosage of D-E rabies vaccine recommended for human post-exposure treatment is inadequate.⁷⁴

Dean,¹⁹ in summarizing his opinion regarding D-E vaccine, said: "... there is evidence in animals that duck-embryo vaccine is less antigenic than nerve-tissue vaccine. Properly produced, nerve-tissue vaccines readily pass the Habel and NIH tests for potency whereas duck-embryo vaccine customarily either passes such tests marginally or fails. Preference for duck-embryo vaccine is apparently justified largely because of its greater

freedom from postvaccinal neurologic complications."

Reactions to Rabies Vaccine Treatment

Nerve-Tissue Vaccine. It is recognized that N-T antirabies vaccines occasionally produce so-called neuroparalytic accidents.³⁴ The incidence of serious paralytic reactions to N-T vaccine varies with different reports but appears to approximate one per 4,000 persons treated.^{7,33,50,55,60}

One study produced evidence also that approximately 14 per cent of persons treated with N-T vaccine had electroencephalographic abnormalities during immunization, whereas persons receiving D-E vaccine in the same study did not.²⁶

The neurological complications occurring with the use of N-T rabies vaccine usually do not begin until after completion of the vaccine course. When symptoms such as chills, fever, headache, nausea, vomiting and generalized lymphadenopathy develop during rabies vaccine treatment, vaccine should be immediately discontinued.^{7,32,35} The neurological reactions to N-T rabies vaccine can be classified as: (a) peripheral neuritis, (b) dorsolumbar myelitis and (c) ascending paralysis (Landry's type).³⁵ Reactions of paralytic type seldom develop until after the sixth dose of N-T rabies vaccine, and they may occur as late as two weeks after completion of treatment.³⁵

Cortisone and corticotropin (ACTH) have been successfully used in controlling reactions to both serum and N-T rabies vaccine.^{12,25,37,49} Evidence indicates, however, that these agents interfere with the development of active immunity¹⁴ and additionally may possibly reactivate rabies infection.⁶⁵

Duck-Embryo Vaccine. While D-E rabies vaccine carries less risk of neuroparalytic accident than does N-T rabies vaccine, the D-E product is not devoid of the paralytic factor. MacFarlane and Culbertson⁴⁶ reported that encephalomyelitis developed in two (2.4 per cent) of 83 guinea pigs injected subcutaneously with D-E vaccine suspended in Freund's adjuvants, compared with 21 (or 87.5 per cent) of 24 guinea pigs after injection similarly with rabbit brain suspensions.⁴⁶

A number of severe reactions in man have also been reported in association with use of duck-embryo rabies vaccine.^{3-6,24,41} It is clear, therefore, that D-E vaccine is less hazardous of neuroparalytic accident than is N-T vaccine but that N-T vaccine will evoke the higher degree of protection against rabies infection. When D-E rabies vaccine is used, its lesser effectiveness should be kept in

mind and not fewer than 14 doses, with booster injections* after 10 and 20 days, should be administered.

When antirabies serum is used, N-T vaccine is probably the vaccine of choice and should also be followed with booster injections† after 10 and 20 days.

Care should be exercised in administration of D-E vaccine to persons known to be sensitive to egg material.⁸⁰ In instances where persons incur severe reaction to D-E vaccine, a change to N-T vaccine may permit continuation of the course of treatment.

Pre-Exposure Immunization

From recent studies, it is clear that any of the rabies vaccines used—for example, chick-embryo Flury strain high egg passage (HEP),‡ duck-embryo (D-E)^{1,8,22,59,67} and nerve-tissue (N-T)^{8,10,23}—are capable of eliciting antibody response in treated persons and thereby sensitizing them or preparing them for prompt response to booster injections.

The Flury strain HEP rabies vaccine which was used in numerous pre-exposure immunization studies, was used experimentally only and is no longer available. Only D-E and N-T rabies vaccines are available now. Of the two currently available products, D-E vaccine, while less potent than N-T, will elicit an immune response and thus sensitize or prepare a person for quick response to future booster injections.^{1,8,22,59,67} Since D-E vaccine carries less risk of neuromuscular complications than N-T vaccine,⁴⁶ the former is probably the rabies vaccine of choice for pre-exposure use in persons at high occupational risk of exposure to rabies.⁸⁰

In most studies on pre-exposure immunization, rabies vaccine has been injected intradermally.§ However, wide variations in response, from approximately 30 to 95 per cent of those inoculated responding, have been noted by various workers using the intradermal route.¶ These variations in response were apparently largely due to variations in the administration of intradermal injections.⁵² As a result, injecting larger doses subcutaneously is the method now recommended.^{38,52,80}

The WHO Expert Committee on Rabies, Fifth Report, recommended that a short primary course

*When D-E rabies vaccine is used for the basic course, use of N-T rabies vaccine for booster injections at 10 and 20 days may reduce the risk of allergic reaction.

†WHO Expert Committee on Rabies, Fourth Report (1960)⁷⁹ recommended use of D-E vaccine for booster injections when N-T vaccine is used for the basic course of treatment.

‡Reference Nos. 8, 10, 23, 56, 57, 59, 61, 67.

§Reference Nos. 1, 8, 10, 22, 23, 56, 59, 61, 67.

¶Reference Nos. 1, 8, 10, 22, 52, 56, 59, 61, 67.

of two to three inoculations of 1 ml of reconstituted D-E rabies vaccine be administered deep subcutaneously in the upper arm at one month intervals. The primary course should be followed by a single booster inoculation six months later.⁸⁰

Since individuals vary in their response to primary immunization it is desirable that a serum specimen (5 to 10 ml) be collected 30 days after the booster injection and submitted to a laboratory for a serum neutralization test to determine the level of antibody response. If antibody response has not been elicited, booster inoculations should be continued until response is obtained. The submission of serum for neutralizing titer determination should be arranged for in advance through the local county health department and the California State Department of Public Health.

The WHO Expert Committee on Rabies, Fifth Report, recommended that booster inoculations be given at one- to three-year intervals as long as the individual remains at risk.⁸⁰ Not enough information is available to provide a basis for firm recommendations as to the best procedure to follow when an immunized person who has demonstrated immune response in the past is exposed to rabies. The WHO Expert Committee on Rabies, Fifth Report, however, suggested that on mild exposure one dose of rabies vaccine be given and that on severe exposure five doses be given, followed by a booster dose 20 days later.⁸⁰ Observed antibody response to booster injections has been prompt—significant rise in titer within four to eight days in persons who have had previous antibody response to rabies immunization.⁸

Re-treatment

It has been found that a single dose of potent rabies vaccine given to persons who have received a course of rabies vaccine as long as 15 to 25 years previously, results in prompt and significant antibody rise^{8,22,23,52} within four to eight days.⁸ The questions here of course are those of verification of previous rabies vaccine treatment, the potency of the vaccine used for previous treatment and the antigenic response of the individual thereto.

Until 1939 there was no practical method of testing rabies vaccines for potency.³⁰ When standard test procedures were developed,^{30,75} it was found that most rabies vaccines produced in the United States lacked potency.³⁰ A similar situation existed with regard to low potency of D-E rabies vaccine when tested by Dean and Sherman in 1962.²¹ It should also be noted that if combined

antirabies serum and rabies vaccine were used, the antigenic response of the individual might be impaired in some degree, particularly if unusually large doses or multiple doses of serum were administered or if less than 14 doses of vaccine plus booster injections (recommended at 10 and 20 days after completion of the 14 dose series) were administered.

If, however, an individual has demonstrated proved immune response to post-exposure treatment or a pre-exposure course of immunization within the past two to three years, the WHO Expert Committee on Rabies, Fifth Report, suggested that in the event of a mild exposure one booster dose should suffice, and for several exposures five doses with a booster dose 20 days later.⁸⁰

Laboratory Diagnosis of Rabies

Fluorescent Rabies Antibody (FRA) Test. This test is a new and important development in rabies diagnosis.^{27,28,45,47} In an experienced laboratory it is fast (overnight as used in the California Department of Public Health laboratory) and the reliability of the test is such that a negative report can be expected to weigh heavily for a decision not to treat a person who has been bitten.^{47,80}

In the California Department of Public Health laboratory over 4,230 specimens routinely submitted for rabies examination between October 1959 and September 1962 were comparatively examined, using the FRA test, microscopic examination for Negri bodies and mouse inoculation test.⁴⁸ Of the total number, 363 were reported positive for rabies, 361 (99.4 per cent) being FRA positive, 357 (98.3 per cent) mouse positive and 239 (65.8 per cent) Negri body positive. Six specimens positive to the FRA test, including four in which Negri bodies were demonstrated, were negative on mouse inoculation. Two specimens initially reported negative to the FRA test were positive on mouse inoculation. On careful reexamination of additional slides from the foregoing two specimens, using the FRA test, a few scattered foci of specific fluorescence were found.^{45,48}

The FRA test was adopted as the standard examination procedure for rabies by the California Department of Public Health in January 1963.^{16,45} From January 1963 through October 1964, nearly 4,000 additional specimens were examined by the FRA test. Of this number, only two specimens initially reported negative to the FRA test were found positive on mouse inoculation. Reexamination of multiple smears of these two specimens (from a

dog and a horse) by FRA revealed trace amounts of specific fluorescence.⁴⁵

In the light of nearly five years of experience in California Department of Public Health laboratory, the FRA test is considered to be highly (99.95 per cent) reliable. The examination results can be reported by that laboratory within 24 hours. The presence or absence of Negri bodies in the specimen is no longer of concern and it is no longer necessary to withhold a final laboratory report for two weeks or longer while awaiting the results of mouse inoculation. The FRA test results, be they positive or negative,* may be used by physicians and public health officials to determine promptly the need for antirabic treatment of persons exposed to an animal suspected to have rabies.⁴⁷

The FRA test is reliable with fresh, frozen or glycerinated specimens and may also be used to examine salivary gland material.^{18,27,28} The efficiency of the test on salivary gland material is still under investigation, however.

Microscopic Examination for Negri Bodies. This examination procedure is rapidly being supplanted by the FRA test in local health laboratories in California (22 of a total of 41 local health department laboratories in California were utilizing the FRA test as of 31 December 1965).

The presence of Negri bodies is pathognomonic of rabies infection. The absence of Negri bodies, however, does not rule out rabies infection. Wide variations occur in the relative frequency of Negri bodies found in the various species of rabid animals. The variations in the frequency of Negri-positive specimens examined by the California Department of Public Health during the 11-year period 1950-1960 are shown in Table 3.

The microscopic examination has been replaced by the FRA test as the routine diagnostic procedure in the California Department of Public Health laboratory.¹⁶

Mouse Inoculation Test. This test was previously performed by the California Department of Public Health laboratory routinely on all specimens in which Negri bodies could not be found or on which examination could not be satisfactorily performed due to the unsuitable condition of the specimen. Its use has been supplanted by the FRA

*In making decision *not to initiate* or to *stop* antirabic treatment in an exposed person based upon a negative FRA test, consideration should be given to the volume of positive rabies material being seen by the laboratory and the frequency of positive specimens missed by the laboratory in the past. In the case of small laboratories, local public health laboratories where relatively few positive specimens are seen—it is suggested that, where possible, material be forwarded to the California Department of Public Health for confirmation.

test.¹⁶ Mouse inoculation will usually be attempted, however, in instances where the condition of specimen precludes reliable testing by the FRA procedure.

The incubation period in inoculated mice developing rabies may range from five to twenty-three days. The average incubation period in the California Department of Public Health laboratory has been approximately 12 to 14 days.* Inoculated mice are routinely observed for 28 days before a negative report is rendered.

Serum-Virus Neutralization Test. This test is used to identify rabies virus. It has been used in the California Department of Public Health laboratory in instances where typical Negri bodies could not be demonstrated in inoculated mice which were dying, to establish if the pathogenic agent were rabies virus. Its use has largely been replaced by the FRA test.¹⁶

The technique, however, is currently used to determine the development of specific neutralizing antibody titer in persons administered pre-exposure or primary courses of rabies vaccine using serum drawn from the individual 30 days following administration of the booster inoculation (See section on Pre-Exposure Immunization).

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CORRECTION

In the article, "Acute Myocardial Infarction in Los Angeles County," by L. Julian Haywood, the figures for the Centinella Valley Community Hospital were incorrectly reported in Table 1. The correct data are as follows:

TABLE 1.—Data From Myocardial Infarction Survey—Hospitals of 95 or More Beds in Los Angeles County

| Hospital | No. of Beds | Data on Infarction and Coronary Insufficiency | | | | Data on Special Care Units | | |
|-------------------------------|----------------|--------------------------------------------------|----------------|--------|-------------------------|----------------------------|------------|------------------|
| | | Condition | Total Cases | Deaths | Mortality (Per Cent) | Beds In ICU | Has CCU | Planning CCU? |
| Centinella Valley Comm. Hosp. | 150 | AI | 218 | 29 | | | | |
| | | ACI | 128 | 9 | | | | |
| | | Total | 346 | 38 | 10.9 | 6 | No | No |

AI = Acute infarction (definite or probable)

ACI = Acute coronary insufficiency

ICU = Intensive care unit

CCU = Coronary care unit

This would also change the figure for the total deaths reported for all the hospitals included in the survey to 2,261 instead of 2,441.

Acoustic Trauma from Rock-and-Roll Music

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■ *Analysis of certain measurements of noise levels and frequency distributions in two rock-and-roll music establishments indicated that this program material can produce temporary auditory threshold shifts and is of an order that has been recognized as entailing risk of permanent ear damage.*

IN A COMPARISON of the auditory acuity of Americans with that of a Sudanese tribe, Rosen and coworkers⁶ observed that what we term "presbycusis"^{1,3} may be partly attributable to the cumulative effects of the environmental noise which is indigenous to western civilization. The study here reported deals with contemporary teenage music as one possible source of ubiquitous, permanent, cochlear injuries.

Presented herein are the results of the analysis of a series of measurements of sound levels and spectra obtained in two typical San Francisco Bay Area rock-and-roll establishments frequented almost exclusively by teenagers and young adults, of whom many fall into a group popularly designated as "hippies."

The musical material evaluated was produced by two groups of young males performing on stages. The main instruments used were amplified guitars and the percussion group. There were some vocal refrains. In both places these sounds were detected by multiple microphones, were strongly amplified, and were reproduced through two large

theater-type speaker systems, one at each end of the stage. The music, which was characterized by very strong rhythmic patterns, varied harmonic coloration, and simple themes with variations, presented a dynamic range between forte assai and fortissimo. The audiences favored listening over dancing, and the area between the speakers near the stage seemed to be preferred. The acoustic output was controlled by a sound engineer in the larger of the two establishments, but in the smaller hall, where the sound levels were found to be higher, there was no such supervision.

Method of Measurement

For purposes of this study, at multiple stations in each hall recordings were made of the noise generated during live musical performances. Used for the recordings were a one-inch condenser microphone, a cathode-follower amplifier, a sound level meter, and a portable tape recorder.* The entire system was calibrated immediately before the test recordings with a piston phone acoustical calibrator.† A recording of 50 to 100 sec. duration was then made of the noise at each station in each hall.

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Presented before the Section on Otolaryngology at the 96th Annual Session of the California Medical Association, Los Angeles, April 15 to 19, 1967.

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*Condenser microphone, 1-inch Bruel & Kjaer, Model 4131; cathode follower, Bruel & Kjaer, Model 2630; sound level meter, Bruel & Kjaer, Model 2203; magnetic tape recorder, Nagra NTBH, Model III.

†Piston phone, Bruel & Kjaer, Model 4220.

These recordings were analyzed in the laboratory using a magnetic tape recorder, a sound level meter, an octave band filter, a graphic level recorder and a statistical distribution analyzer.‡ The laboratory equipment was calibrated with the field equipment by means of a calibration signal recorded just before the test. The recording of each individual station was then played back through the octave band filter and sound level meter into the graphic level recorder. Graphic level tapes were made for the overall noise level at each station. The statistical analyzer was set to count for a period within the duration of the test recordings. The statistical data were derived by a mechanical switching device attached to the writing arm of the graphic level recorder. The data for statistical analysis was recorded in two modes: the first was a standard distribution showing the amount of time the sound level fell within the bounds of each intensity band; the second mode recorded the time spent at or above each fixed intensity level. The cumulative distribution data were used as a basis for octave band spectra and other further analysis.

By dividing each intensity band count into the total period count, the percentage of time spent at or above each fixed level was determined. This data was the base for octave band spectra of six duration lengths: 10 per cent, 20 per cent, 30 per

cent, 40 per cent, 50 per cent and 60 per cent. These spectra were analyzed by a computer to

ABBREVIATIONS AND SYMBOLS

| | |
|--------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| db: | Decibel. |
| Dba: | A scale of loudness based upon the "A" scale of a standard sound level meter, in which an electronic weighting network compensates for the poor sensitivity of the human ear to low frequency sounds. |
| Dbc: | The weighted scale of loudness which is measured in terms of the almost flat frequency response of the sound level meter and microphone between 20 and 10,000 Hz. |
| DbLin: | The unweighted sound-pressure levels between 20 and 20,000 Hz. |
| Hz: | Cycles per second. |
| NOY: | A unit of perceived noisiness based upon the arbitrary assignment of a value of 1 to the perceived loudness of random noise in the band of 910-1090 Hz at 40 db re .0002 microbar. |
| PHON: | The logarithmic counterpart of the SONE. |
| PNdB: | The unit of perceived noise levels based upon the arbitrary assignment of a value of 1 to the perceived loudness of frequency bands between 20 and 10,000 Hz at 40 db re .0002 microbar. |
| SIL: | The speech interference level of environmental noise is derived from the arithmetic mean sound level measurements in decibels in the octave frequency bands: 600 to 1200 Hz, 1200 to 2400 Hz and 2400 to 4800 Hz. |
| SONE: | A linear unit of loudness based upon subjective equivalency to the loudness of a simple tone of 1000 Hz at 40 db above the normal human threshold. |

‡Magnetic tape recorder, Roberts, Model 990; octave band filter, Bruel & Kjaer, Model 1612; graphic level recorder, Bruel & Kjaer, Model 2305; distribution analyzer, Bruel & Kjaer, Model 4420.

| TABLE 1. — <i>Frequency Compilations at Center of Octave Band, in Hz</i> | <i>Noise</i> | <i>Levels</i> | <i>DbLin</i> | 63 | 125 | <i>Frequency in Cycles per Second</i> | | | | | |
|----------------------------------------------------------------------------------|----------------------------------------------------------|---------------|--------------|-----|-----|---------------------------------------|-----|-------|-------|-------|-------|
| | | | | | | 250 | 500 | 1,000 | 2,000 | 4,000 | 8,000 |
| | State of Calif. Ear Damage Risk Criteria | | ... | 110 | 102 | 97 | 95 | 95 | 95 | 95 | 95 |
| | At Hall A— | Avg. | 109 | 102 | 103 | 105 | 102 | 101 | 102 | 92 | 79 |
| | Center of | Min. | 105 | 92 | 95 | 98 | 95 | 96 | 95 | 87 | 73 |
| | Auditorium | Max. | 111 | 105 | 109 | 109 | 105 | 104 | 104 | 95 | 82 |
| | At Hall B— | Avg. | 118 | 107 | 112 | 113 | 112 | 106 | 95 | 91 | 83 |
| | Center of | Min. | 114 | 103 | 109 | 112 | 107 | 103 | 92 | 88 | 78 |
| | Auditorium | Max. | 122 | 109 | 116 | 116 | 119 | 109 | 100 | 96 | 87 |

TABLE 1.—Frequency
Compilations at Center
of Octave Band, in Hz

| | | Noise | Levels | DbLin | NOYS | PNdB | SONES | PHONS | SIL | dBc | dBa |
|----------------------------------------------------------|------|-------|--------|-------|------|------|-------|-------|-----|-----|-----|
| State of Calif. Ear Damage Risk Criteria | | ... | ... | ... | 206 | 117 | 196 | 116 | 95 | 111 | 102 |
| At Hall A— Center of Auditorium | Avg. | 109 | 235 | 119 | 209 | 117 | 209 | 117 | 98 | 110 | 106 |
| | Min. | 105 | 147 | 112 | 126 | 110 | 126 | 110 | 93 | 103 | 100 |
| | Max. | 111 | 285 | 122 | 260 | 120 | 260 | 120 | 101 | 114 | 109 |
| At Hall B— Center of Auditorium | Avg. | 118 | 301 | 123 | 287 | 122 | 287 | 122 | 97 | 118 | 111 |
| | Min. | 114 | 246 | 120 | 230 | 119 | 230 | 119 | 94 | 115 | 107 |
| | Max. | 122 | 435 | 128 | 419 | 127 | 419 | 127 | 102 | 122 | 116 |

TABLE 2.—Noise of
Rock-and-Roll Groups as
Measured by Subjective
Criteria

obtain noise level ratings in SONES, PHONS, NOYS, PNdB, SIL, dBa, and dBc.

Results

Tables 1 and 2 contrast the rock-and-roll sound measurements with the State of California ear damage risk criteria.⁸ In each of the data computations and in almost all of the octave band center frequencies the noise levels at the stations shown* exceed these established levels.

Discussion

It is not within the scope of this paper to re-establish those features of noise which make it potentially harmful to the cochlea. This has been done thoroughly and well by many investigators.^{2,4,5,7,9}

One may predict that noise greater than 92 decibels in sound pressure composed of frequencies primarily between 500 and 8,000 Hz and sustained for a period of one hour will produce as much as 40 decibels threshold shift in the area of 4,000 Hz in approximately 10 per cent of the ears exposed, no measurable shift in another 10 per cent, and between 5 and 30 dB shift in the remaining 80 per cent of ears.

*The station shown is in the center of each auditorium.

We believe that we have demonstrated that the noise levels produced by some live rock-and-roll bands with the aid of high amplification unmistakably exceed those considered safe for prolonged exposure. Attenuation of the amplification to safe levels would substantially reduce the risk of ear injury in the audience and performers and, in the opinion of the authors, would still permit enjoyment of the musical material.

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The Intensive Respiratory Care Unit

An Approach to the Care of Acute Respiratory Failure

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■ *An organized approach for the management of acute respiratory failure in an intensive general care unit utilizes a team of consultants including a general physician, a surgeon, respiratory care nurses, physical therapists and a blood gas technician. Because this team provides consultation and technical assistance in respiratory care and provides the equipment as well as the monitoring of care, this approach is suitable for any hospital interested in the management of acute respiratory emergencies.*

THE DEVELOPMENT of an organized team approach for the management of acute respiratory failure has been successful in improving the recovery rate of patients with acute respiratory failure from a variety of causes including chronic airway obstruction, surgical states, neurological problems and poisonings. Several units have been developed which bring together, in a physically distinct area, the disciplines of internal medicine, surgery, intensive nursing care and pulmonary physiology.^{2,4,6,7,9} Although each has been successful, it is recognized that, as described, they might not be administratively suitable or economically feasible for the vast majority of general medical and surgical hospitals, whether academically or community oriented. Hence the purpose of this report is to describe the organization and role of a consulting respiratory care unit which functions within a general intensive care area. The approach to care described herein has been found to be suitable for hospitals which operate a general intensive care unit.

The personnel and equipment for the respiratory

care consulting service is housed in a laboratory 18×36 feet which adjoins the general intensive care unit (Figure 1). This laboratory contains the ventilatory equipment for respiratory care, endotracheal and tracheostomy tubes, adapters and all the ancillary devices necessary for the management of patients with acute respiratory failure. The availability of instruments for blood gas analysis is fundamental for the diagnosis and management of respiratory failure; this equipment is maintained in the unit. A full-time blood gas technician calibrates and uses the equipment during daytime hours and physician consultants in respiratory care also avail themselves of this equipment at any time of day or night. A nurse specialist in respiratory care has administrative responsibilities for the functioning of the laboratory. This nurse has been fully trained in all aspects of inhalation therapy and supervises this facet of care within the intensive care unit. An aide is responsible for the cleansing and maintenance of the respiratory care equipment. The final responsibility for the supervision of professional aspects of the unit rests with a physician trained in respiratory care.

Patients are cared for in an adjacent 12-bed intensive care medical area which includes facilities for electrocardiographic and hemodynamic monitoring. Postoperative and trauma cases are

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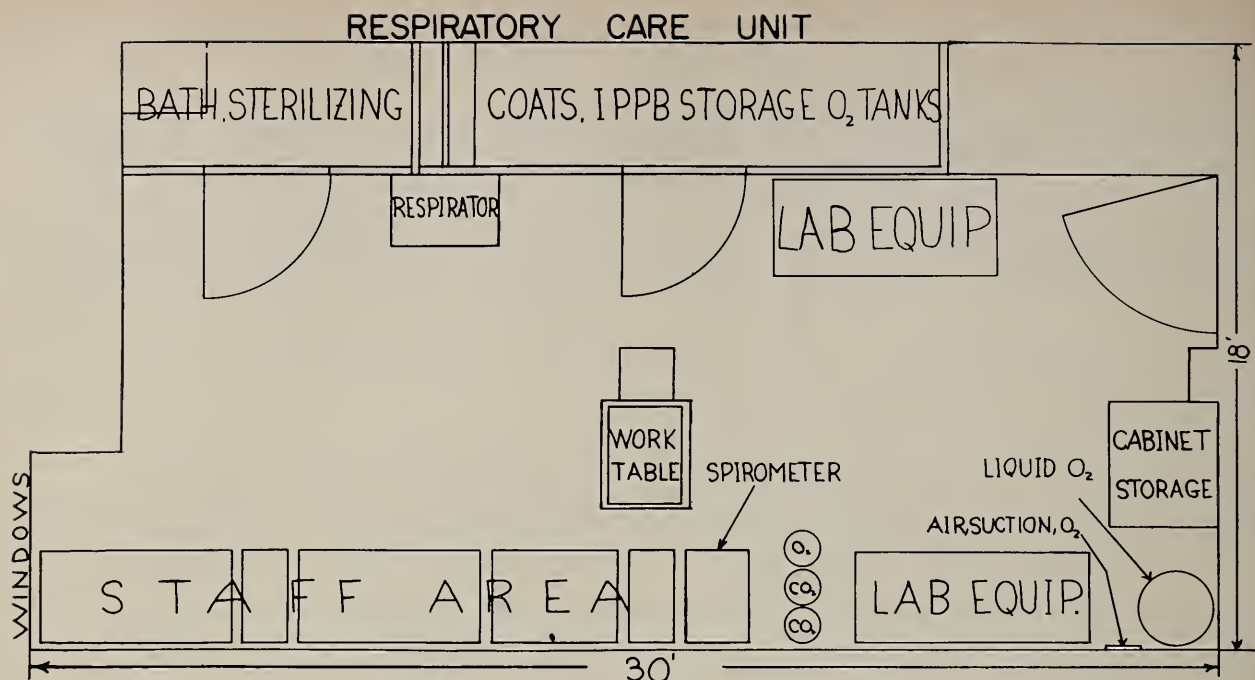


Figure 1.—Floor plan of the respiratory care laboratory. The laboratory houses the ventilators, (IPPB = intermittent positive pressure breathing) blood gas equipment and other monitory equipment, and provides office space for the respiratory care personnel. All facilities necessary for maintenance and sterilization of equipment are kept in the unit. The two CO₂ tanks are to supply the two concentrations needed for Astrup determination. The oxygen tank is used for calibration of the oxygen electrode. (Reproduced from *Medical Clinics of North America*³ by permission of the W. B. Saunders Company, Philadelphia.)

managed in a similar adjacent surgical area.

The purpose of the respiratory care unit is to provide personnel and equipment for the management of respiratory failure in both acute and extended care. The unit personnel provides consultation to the house staff (or private) physicians involved in the daily care of patients. When acute respiratory failure is suspected by clinical criteria,³ an arterial puncture—a simple procedure easily mastered by any physician⁸—is immediately performed by the physician in charge. In acute respiratory emergencies or after the diagnosis of respiratory failure has been confirmed in the laboratory, patients are transferred to the intensive care areas for bronchial hygiene, controlled low flow oxygen therapy or total ventilatory assistance as each requires.

The details of management of acute respiratory failure are beyond the scope of this communication. In principle, the management of respiratory failure can be divided into three phases: (1) emergency care and resuscitation, (2) definitive care and (3) early rehabilitation.³

In brief, profound hypoventilation or apnea is a medical emergency. Immediate steps must be taken to improve alveolar ventilation and oxygenation or the patient will die in a matter of minutes.

Some form of immediate ventilation is mandatory—mouth-to-mouth respiration or mouth-to-tube breathing or assisted ventilation using the self-inflating resuscitation bag (for example, Ambu or Hope resuscitation bag) with a mask and oral pharyngeal airway or with an endotracheal tube. During this aspect of respiratory care, automatic ventilators have no role. After resuscitation has been achieved and ventilatory needs are relatively constant, supportive measures are introduced to continue adequate oxygenation and carbon dioxide elimination. Artificial ventilators are employed at this point. In addition, efforts are directed toward the management of the underlying causes of disease—that is, precipitating events which, at least theoretically, may be reversed and improve the chances for survival.

Most commonly, acute infections, retained secretions, bronchospasm, heart failure, debility, trauma and poisonings are the precipitating events in acute respiratory failure. In chronic airway obstruction, acute infections are almost always present. Antibiotics are given from the start—ampicillin, tetracycline or high dosage penicillin directed at the most commonly involved invading bacteria (*D pneumonia* and *H influenza*). If the patient has previously been receiving antibiotic therapy and

Gram-negative rod infection is suspected, other appropriate antibiotics including kanamycin, polymyxin B or cephalothorin are administered.

A problem with retained secretions is present in almost all kinds of respiratory failure. Meticulous nasotracheal suction, suction via an endotracheal tube or tracheostomy care is fundamental for successful management. Effective removal of secretions demands atraumatic and aseptic suctioning techniques. Secretions must be removed as often as necessary. This may be as frequently as every 15 minutes, and most certainly no less often than every one to two hours. Use of the gloved hand technique and application of suction only during withdrawal of the catheter are well established principles. For removal of secretions a tracheostomal opening is usually more satisfactory than suctioning through an endotracheal tube.

In chronic airway obstruction, an element of smooth muscle spasm or bronchomucosal edema is often present. For this reason, we use parenteral xanthine (aminophyllin, 500 mg in 500 ml of water every six hours) and/or inhaled isoproterenol 1:200 or racemic epinephrine with a 1:1 or 1:2 further dilution with water to combat the reversible factors of airway obstruction. Inhalations of a bronchodilator agent may be needed as often as every one to two hours.

Congestive heart failure can precipitate acute respiratory failure.¹ On the other hand, congestive right heart failure may be a manifestation of impaired ventilation and oxygenation. Measures to clear the airways, to provide adequate oxygenation and to eliminate carbon dioxide are important principles in the management of right heart failure, which is frequently precipitated by reactive pulmonary hypertension in response to both hypoxemia and acidemia. In cor pulmonale with congestive heart failure, cardiac glycosides and rapidly acting diuretic agents may help greatly.

The pronounced debility in patients with chronic airway obstruction remains a profound problem. Managing it involves physical rehabilitation, which will be discussed later.

The effects of chest trauma often require appropriate tube drainage and occasionally surgical intervention if there is massive hemothorax or fracture of the bronchus. The crushed "flail chest" is best stabilized by employing total ventilatory support, usually with a volume cycled ventilator.

When respiratory failure occurs solely as a manifestation of poisoning, the patient should re-

ceive ventilatory support until the poison is removed either by hemodialysis or by the patient's own renal function. In the event of potentially reversible neurologic emergencies, with the administration of cholinergic drugs one can hopefully await recovery in the case of Guillain-Barré syndrome and often in acute myasthenia crisis.

Steps in the care of a patient with respiratory failure are briefly cited herein to clarify the role and responsibility of the members of the respiratory care team.

Morning rounds are conducted by the entire staff including physicians, nurses and technicians to supervise and to review the conduct of respiratory care, to check on the adequacy of equipment function and to maintain close rapport with the patient. In addition to formal rounds once daily, individual bedside checks are made frequently throughout the day by physicians and nurses of the team.

Communication with the attending staff is of great importance when one considers that the role of the consulting respiratory care unit is to supervise and adjust the ventilators as may be required to meet the changing demands for ventilation and gas exchange. Suggestions for the management of the underlying features of the disease, as previously discussed, as well as efforts toward rehabilitative aspects are all the responsibility of the consulting unit. Infections, disease problems, correction of coexisting acid-base derangements, management of cardiac arrhythmias and congestive heart failure are all included in the total management of the patient, and advice in this care is one of the duties of the consulting respiratory care team.

Since it is a consulting service, members of the respiratory care unit do not write orders unless absolutely necessary in emergency care. Close communication with the attending staff is mandatory. For this reason, oral and written communications are provided whenever a significant observation is made. This policy not only insures immediate correction of potential or existing problems, but it is also important in the training of physicians.

During the definitive therapy phase of acute respiratory care, ventilation and gas exchange are supported with equipment which provides the work of breathing. Treatment meanwhile is directed to the underlying reversible features of the disease causing the need for respiratory care.

When the patient can maintain adequate ventila-

tion on his own (as judged by bedside measurements of ventilation and blood gases), use of the ventilator is stopped for a trial period, additional oxygen being given in the inspired air. Patients are ambulated early in their course in order to maintain muscle tone and conditioning and to avoid the many complications arising from prolonged bed rest. If mechanical aid to ventilation may still be needed during early ambulation, it can be provided with the self-inflating bag still attached to the tracheostomy tube. Supplemental oxygen is often necessary even after spontaneous ventilation is sufficiently restored to permit closure of the opening in the trachea. It can be given by conventional means or, more easily, with portable oxygen equipment, which the patient can carry. As was mentioned previously, the responsibility of the respiratory care unit includes not only the early phase of rehabilitation but extended care, for success in respiratory emergencies is meaningless unless the complete care which leads to physical rehabilitation can be provided.

The potential for rehabilitation of patients who are threatened by episodes of acute respiratory insufficiency has only recently been stressed.⁵ Nearly 70 per cent of them can recover from the emergency, be transferred to ordinary wards and, if rehabilitation efforts are successful, ultimately recover to a comfortable home existence. For this reason the physical therapist plays an important part in the respiratory care team. Physical therapists should participate early in the care of patients with respiratory failure. Their role includes breathing retraining and graded exercises, including walking and general physical reconditioning, particularly in the case of patients with chronic airway obstruction who may require a prolonged recovery period.

The final stage of extended care includes the role of the public health nurse. She maintains liaison with the medical staff and supervises the still necessary (and often long-term) bronchial hygiene and inhalation therapy in the home.

Results

The results in 285 cases in which intensive care was required for respiratory failure from various causes, are shown in Table 1. An over-all salvage rate of 66 per cent was obtained despite the many desperate clinical situations encountered.

Discussion

The organizational structure of the unit and

TABLE 1.—Data on 285 Patients Dealt with by an Intensive Respiratory Care Team in a General Hospital

| Principal Diagnosis | Survived | Died* | Total |
|-------------------------------------------------------------------------------------|----------|-------|-------|
| 1. Severe Chronic Airway Obstruction (1st episode of respiratory failure) | 42 | 14 | 56 |
| 2. Other Pulmonary Disease | | | |
| a. Massive pneumonia | 3 | 4 | 7 |
| b. Interstitial fibrosis | 7 | 0 | 7 |
| c. Moderate chronic airway obstruction | 23 | 2 | 25 |
| 3. Surgical Problems | | | |
| a. Postoperative states | 55 | 30 | 85 |
| b. Trauma | 16 | 8 | 24 |
| c. Burns over 75 per cent of body area | 0 | 5 | 5 |
| 4. Poisonings | 17 | 8 | 25 |
| 5. Neurological emergencies | 19 | 11 | 30 |
| 6. Miscellaneous (includes cardiac arrest from various causes) | 7 | 14 | 21 |
| TOTAL: | 189 | 96 | 285 |

*Includes deaths from all causes during hospitalization.

the methods of care described do not make use of any new principles of respiratory care. They are simply the development of an organized team approach to specialized aspects of respiratory care suitable for general hospitals. In this era of specialization which employs the technical advances of new equipment for the care and monitoring of patients, highly trained personnel are needed. The development of intensive care units has proved economically feasible for the management of patients in medical emergencies of all types. This is also the case with acute respiratory failure.

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Advances in Multiphasic Screening and Testing

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■ *The multiphasic testing center of the future will probably be used both for periodic screening tests and for referrals by practicing physicians. Recent widespread interest of several branches of the Federal Government in multiphasic screening stems from the possibility that, through its use, the enormous cost of chronic illness to the country may be reduced.*

Recent advances in automation and the storage, retrieval, and analysis of data by computers make it economically feasible to obtain much more information about the patient's health than ever before. New instrument developments include both screening and diagnostic analysis of electrocardiograms by computers, analysis of heart sounds by computer, and a wide variety of other physiological and biochemical instruments.

To allow for the inclusion and evaluation of these new procedures, a number of multiphasic testing centers will be needed which can do both research and routine testing. Close cooperation between the medical profession, the public health services and industry will be needed to best serve both the public and the medical profession.

ALTHOUGH IT IS generally agreed that screening tests, as they are looked upon at present, are not diagnostic tests, one reason for performing the tests is to select, out of a large number of apparently healthy persons, those who have a relatively high probability of having the disease or diseases being sought. Definitive diagnostic procedures then can be performed. Thus, while it may not be considered a diagnostic procedure in and of itself, screening is the preliminary step in a procedure which has as its

end objective the establishment of a diagnosis. Furthermore, some of the tests being used in screening centers are the same tests that are performed by diagnostic clinical laboratories today. An example is the use of automated analyzers to run a battery of biochemical tests. New methods and tests will be developed, some of which will provide information more nearly diagnostic in nature, such as computer analysis of electrocardiograms.

Since tests of this kind are included in screening centers, it appears quite possible that such centers might also be useful as referral laboratories for individual physicians. Thus, instead of sending a patient to several different laboratories to obtain a

Presented at the Second General Meeting at the 96th Annual Session of the California Medical Association, Los Angeles, April 15 to 19, 1967.

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variety of tests such as x-ray studies, clinical chemical determinations, and electrocardiograms, the physician could send his patients to a screening center and have all the tests performed in one place. This should result in a reduction in cost to the patient and yet should give the physician the reliable information he needs—provided the screening centers use accepted test procedures and are organized to take advantage of automated equipment and data handling by computers. For example, a significant portion of the persons who go through the Permanente multiphasic screening unit are referred by private physicians. In fact, such centers should probably be referred to as multiphasic testing centers or multitest laboratories⁵ which could be used either for screening or diagnostic work.

Through multiphasic screening tests on the same persons over long periods, significant trends might be found which could lead to a prediction of impending onset of a chronic disease. The physician might then begin preventive measures based on the trends established by the screening procedure, without further definitive testing. In this way the screening program may assume somewhat more of a diagnostic nature.

The use of screening procedures in medicine is not new by any means. In a recent survey of the literature, it was found that almost 1,500 papers on this general subject have been published in the past 10 years alone. The papers deal with all aspects of screening, from philosophy and principles to detailed results of many programs. A recent United States Senate subcommittee investigating the use of multiphasic screening for the early detection and prevention of chronic disease produced a report¹³ containing more than 600 pages of testimony by a large number of experts in the field.

The present communication will be limited to a brief review of the subject, a discussion of recent advances in instrumentation and procedures which may have a strong influence on the future of medical screening and testing, and a view of future possibilities.

The Role of Screening in Medicine

Screening is the application of a methodical process to a large group of persons in order to separate that group into smaller individual groups having certain characteristics. As used in medicine, screening is usually thought of as the examination of a large number of apparently healthy persons in

order to find out who among them has a high probability of having some specified abnormal condition. The winnowed group is then examined with definitive procedures to aid in arriving at a diagnosis. In this sense there is a distinction between screening tests and diagnostic tests, but it should be noted that even with tests that are generally looked upon as "diagnostic," the actual diagnosis is made by a physician from information obtained from the physical examination and history as well as from tests.

In general, the abnormal conditions discovered by the screening procedure are of two types. In some cases, the person being tested may have a disease at a stage where there are overt clinical symptoms and signs; in others the findings may be only indicative of a pre-clinical stage. For persons of the latter group, preventive or therapeutic measures may prevent the actual disease or, more frequently, may keep serious complications from developing. At least in part the present wide interest in multiphasic screening is attributable to the preventive possibilities. At a recent United States Senate subcommittee hearing¹³ the total economic cost of illness to the country was estimated to be between 50 and 90 billion dollars annually. It was further estimated that if nothing were done to reduce the incidence of chronic disease in the next 10 years, the cost would increase until by 1975 the annual cost could be as high as 180 billion dollars. The possibility that this tremendous financial burden may be reduced by early detection of chronic illnesses and subsequent prevention of the debilitating aspects of such diseases is partly responsible for the interest of the Federal Government in multiphasic screening.

At one of the subcommittee's hearings, Robert H. Ebert, M.D., dean of Harvard Medical School, discussing the problem of assigning priorities in programs contributing to the nation's health, said that "no one would argue that disease prevention is the most valuable contribution." Dean Ebert then pointed out the great advances that have been made in the prevention of contagious diseases and their sequellae through the development of vaccines for poliomyelitis and a host of other diseases. Turning to the problem of the detection of disease, Dean Ebert said that "multiphasic screening is a more efficient and economical method of case finding than the categorical approach."

An extension of multiphasic testing involves the use of examinations performed periodically to es-

establish trends. Decisions to begin some form of treatment may be based on changes in the many factors being measured rather than on a single deviation from a normal range. This has been referred to as "predictive medicine" or "predictive health," and the process is in early stages of evaluation in several centers. George James, M.D., dean of Mount Sinai School of Medicine, in giving testimony at the previously mentioned Senate subcommittee hearings, said that "many of these same tests can also detect changes so early that they are more nearly indicators of a possible risk factor than a developing disease."

Another form of screening in medicine is used to identify groups of persons who have a high probability of having *no* disease or defect, as in the case in screening people for certain occupations or as life insurance risks. In this case, the screened group is usually not subjected to further definitive testing unless the initial results are questionable.

Still another form of screening may be used in epidemiological studies where the primary goal is to obtain information. Each of these applications of screening may have certain requirements which could influence selection of the type of test to be used and the screening level.

It is to be strongly emphasized that when tests which are aimed at the early detection of disease are used in the screening program, these tests are only one phase of a two-phase plan. The second phase consists of performing whatever further tests and examinations may be necessary for the physician to arrive at a diagnosis. To perform only the screening phase is useless and may be harmful.

Review of Screening Programs

As the principles, procedures and philosophy of screening for health and disease have been thoroughly discussed and widely published,^{1,3,11,12} this communication will only briefly review types of screening programs and consider recent advances and their bearing on the present and future practice of medicine.

Single Test Screening

Single test screening in which a single test is used to screen for a specific disease has been in use for many years. Chest x-ray films for tuberculosis and drives for the detection of diabetes, glaucoma, cervical cancer, syphilis and other diseases are all well known and have been shown to be of definite value. It soon became evident that it would be more eco-

nomical to perform more than one test at a time and multiple tests to screen for a number of diseases came into being. While most of the screening of the future will probably be of the multiple or multiphasic type, some single test screening will no doubt still be used in special cases.

Multiple Test (Multiphasic) Screening

In the strictest sense of the word, any program that uses more than one test screening for more than one disease is a multiphasic program. Thus, it is difficult to tell when multiphasic screening came into being. The first person to combine two tests probably started multiphasic screening. In one sense, though, multiphasic screening in medicine far antedates any of the programs that have been referred to here. In fact, the practicing physician himself performs a limited multiphasic screening procedure on each of his patients. For example, suppose a patient sees his physician because of a cough. Does the physician limit his examination to the patient's chest?—not if he follows the training he received in medical school. A medical history is obtained, including past illnesses and family history as well as a history relating to the chief complaint. In the physical examination the physician has been trained to check all medical systems, not just the one pertaining to the complaint. In many cases it is the practice of the physician to get some sort of blood and urine evaluation.

All these procedures serve to alert the physician to possible disease in the patient, whether related to the present complaint or not. This is, in essence, screening. Why have we been trained to make this kind of examination? Certainly one of the reasons is that it is in the patient's best interest provided there is no undue economical burden placed on him or on the physician. This is one of the prime reasons why multiphasic screening or testing is beginning to occupy a more prominent place in medicine. New methods of making measurements and processing the resultant data are beginning to make it economically feasible to obtain much more information about our patients' health, or lack of it, than ever before.

The first overt multiphasic screening program reported in California was performed in 1949 by Canelo, Bissell, Abrams and Breslow.⁴ In this program 945 persons were screened and the screening procedures were two blood tests, two urine tests, an x-ray film of the chest and a brief history. In

1955, Breslow² reported on 16 additional programs which had been carried out in California since the first one in 1949. These 16 programs used as few as two and as many as 12 multiple tests. In 1951 a multiphasic screening program was initiated by the Kaiser Foundation Health Plan and was reported by Collen and Linden in 1955.⁶ This program utilized seven routine tests, a medical questionnaire and several special tests for persons over 40 years of age. Since 1951 the program at Kaiser Permanente under the direction of Dr. Morris Collen has expanded to become one of the most sophisticated programs in the United States today. In 1964 Collen, Rubin and Davis⁷ reported on the advantages of automation and computer analysis in screening. Nine advantages of this approach were delineated, with economy heading the list. A detailed description of the present Permanente testing procedure was given by Collen in 1966.⁵

Many other multiphasic programs have been carried out by various agencies in many other states. Screening programs in at least 11 states, as well as some programs for private groups such as labor unions, were discussed in the previously mentioned Senate subcommittee hearings.¹³

Three years ago the U.S. Public Health Service initiated a 10-year study at the Permanente Multiphasic Screening Clinic to determine the effect of periodic multiphasic screening on the mortality and morbidity of the persons screened. A similar program has been under way at the University of Pennsylvania for some time. In some areas screening clinics are being considered for the poverty programs. The City of Hope National Medical Center recently submitted a proposal to the U.S. Public Health Service for a \$650,000 grant to establish a three-year program using multiple trailer-laboratories to carry out multiphasic screening at the work-site of three trade unions in the Philadelphia-Camden area.

It is fairly evident that in the immediate future there will be an increasing emphasis on utilization of multiphasic screening programs, not only for several programs of the Federal Government but also for use by private groups such as labor unions, insurance companies and industrial employers. Many of these programs will have been established and put in operation long before the answer as to their effect on morbidity and mortality has been established.

New Procedures

Impact of Automation and Computers

It is only by the use of automated methods and data storage, analysis and retrieval by computers that the more ambitious multiphasic programs can be feasible economically. One of the large economic gains comes about through reduction in the amount of labor needed. Furthermore, much of the labor that is required can be done by non-professional and non-technical personnel.

The use of automated systems and computer handling of data has already been mentioned in respect to the Permanente program.^{5,7,8} The group at the Instrumentation Field Station, Heart Disease Control Branch, U.S. Public Health Service in Washington, D.C., has investigated the role of computers in diagnostic centers.^{12,13}

A published description of the present program at Permanente⁵ gives details as to how computers and automated or semi-automated procedures aid in that program. The person screened receives a packet of IBM cards, one for each station he visits. At these stations data is either punched into the card directly (autoanalyzer results) or the card is sense-marked for punch card operations. For tests which still require manual handling or verbal report of visual observations—for example retinal photographs, x-ray films and electrocardiograms—the results are sense-marked by the persons reading the data and are subsequently punched on IBM cards. By the time the person being screened finishes the testing procedure, much of the data have already been processed by the computer and, where indicated, subsequent more definitive diagnostic procedures are scheduled while he is still in the center. The ultimate goal, of course, is to have all the results “on line” so that immediately after the screening is completed, all subsequent procedures can be scheduled. Some of the obstacles to this goal will be discussed later.

Another potential use of computers in multiphasic screening or testing is in the analysis of all the data that are obtained in repeated examinations. These data can be subjected to complex multivariant analytical procedures to search for significant factors which can be used to establish “health profiles” for each person. Changes in these factors or profiles might serve as earlier indicators of impending diseases than we now have. At this stage in the development of multiphasic testing, that potential has not actually been demonstrated. It will be necessary to accumulate such data over a period of

several years before it can be determined if a "predictive" potential can be realized.

New Tests

New test procedures which can contribute to the ultimate success of multiphasic screening and testing are at present in various stages of research, development and evaluation. For the most part these new procedures are based on the use of electronic instrumentation. It is not possible to discuss all of the new tests or testing procedures that are in the process of development. I will mention some of those of which I am aware.

Perhaps more is being done along these lines in the cardiovascular than in other fields. Computer analysis of electrocardiograms has been under intensive study by several groups. One of the best known of these studies is that by Caceres^{9,10} of the Heart Disease Control Branch of the U.S. Public Health Service. He has developed computer programs for the detailed analysis of the conventional 12-lead electrocardiogram. Data acquisition systems are being developed so that the electrocardiogram can be put on magnetic tape in either analog or digital form and the tapes played into computers through the proper conversion systems for analysis. In cases where the analysis is needed on a "stat" basis the electrocardiogram signals can be fed directly to a computer for "on-line" analysis.

An intermediate type of electrocardiogram analysis is also under evaluation. An instrument now being tested consists of a self-contained computer which analyzes a five-lead electrocardiogram and gives an answer as to "within normal limits" or "outside normal limits." This is truly a screening instrument and if the answer were "outside normal," the person screened would then be subjected to a diagnostic electrocardiogram procedure, probably computerized. Such an intermediate system has the advantage that the more complex and detailed analysis is performed only on "positives" (in one screening center this amounts to about 20 per cent of the total number screened).

Another instrument analyzes heart sounds and, through the use of a self-contained computer, presents the results as "within" or "outside" normal limits. The sounds which are outside normal limits are categorized as to whether the abnormality occurs in systole, diastole or as a split second sound. This instrument has been tested on more than 15,000 children and found to be useful. Its application to adults is currently under investigation.

Other new automated procedures are being developed which will give measurements of respiratory function, pulse wave velocity, pulse wave contour and peripheral blood flow, as well as new biochemical measurements such as the amounts of trace metal elements in the blood. Advances in measurement methods in the fields of biochemistry and physiology are under intense investigation and many new procedures will be forthcoming in these fields. More and more emphasis is being placed on obtaining "real time"* data and in certain cases this may involve the use of *in vivo* tests. It may then be possible to utilize more "dynamic" tests rather than tests of single static type. By dynamic tests, I am referring to a "tolerance" test, one which measures the ability of the body to respond to a displacement from the normal level. The glucose tolerance test is an example of dynamic testing in which a measure of the body's ability to handle a glucose load gives much more information than a single measure of a fasting blood sugar. Tolerance tests when the response time is one of minutes may also show promise but would require more nearly real time testing than that for a glucose tolerance test. It soon may be possible to perform hydrogen ion tolerance tests or electrolyte tolerance tests where the response to a small amount of ammonium chloride or to a sodium or potassium load may be determined. Such data may give more information on a person's fluid and electrolyte status than a single test of blood pH, sodium or potassium. Further downstream in time, tests of tolerance to intermediary metabolic components such as lactic acid may be possible.

The new tests discussed above all involve relatively simple types of measurements such as a chemical concentration or analysis of an electrical analog signal.

Other types of tests, some of which are very important and which are used today, have a type of readout that will be difficult to automate. Tests of these types usually require some sort of judgment based on the recognition of complex morphological properties. Examples are x-ray films and stained smears for morphologic study of cells (Papanicolaou stain). While efforts are being made to automate these readouts, it is doubtful that satisfactory methods will be forthcoming in the near future. This means that it will still be some time before it will be possible to have a complete anal-

*"Real time" data—Data that are obtained either continuously or intermittently in such a manner that the results are available with virtually no delay.

ysis of screening tests before the person being screened leaves the screening center.

Multiphasic Screening Research

If the full potentials of multiphasic screening and testing are to be realized, a continuing research program will be needed. As new tests, techniques and data handling systems are developed to the point where they could be economically included in a multiphasic program, some arrangement should be made for their evaluation. Certainly no new procedure should be routinely included in multiphasic programs until such an evaluation is made. One could visualize a limited number of regional centers where such research could be carried out as part of their total program. When these centers show that a new technique is useful, it could then be turned over to other screening or testing centers which are providing a routine service.

The Permanente center evaluates new procedures. For example, a study is under way to investigate the usefulness of performing trace metal concentrations in serum. Such studies may need fairly long periods before a conclusion about their significance can be reached. In addition, it appears advisable that more than one center should be evaluating the same new procedures, as there may be significant differences in the type of populations served by various centers.

It seems reasonable to assume that multiphasic screening or testing will become a standard procedure in certain areas in the field of medicine. In order that these programs can best serve both the public and the medical profession, close cooperative effort between the medical profession, the vari-

ous public health services and industry will be needed.

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Experimental Emphysema

Histologic Changes and Alterations in Pulmonary Circulation

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■ *Detailed study of the pathogenesis of bullous emphysema has been hampered by lack of a suitable animal model of this disease. Prolonged exposure of rats and dogs to elevated partial pressures of oxygen produced a chronic obstructive disease in the lungs of these animals which anatomically resembles bullous emphysema in man. The disease was characterized by extensive bullae formation, alveolar septal destruction, airway obstruction and pronounced circulatory changes. It is suggested that this condition in laboratory animals may serve as a model for the study of pulmonary obstructive disease.*

DURING RECENT YEARS there has been a decided increase in the frequency of emphysema. Goldsmith⁸ reported a 300 per cent increase in the incidence of the disease in California between 1950 and 1958, and in England it is responsible for more fatalities than pneumonia or lung cancer.¹³ Intensive studies of the pathogenesis of obstructive emphysema have been hampered by lack of a suitable animal or "laboratory model" in which to investigate the disorder. Attempts to produce emphysema⁶ have commonly utilized some form of mechanical stress to restrict expiration of air from the tracheobronchial tree and, in general, have been only partly successful. Other methods have brought about septal destruction and disten-

sion of the lung by inhalation of toxic agents such as phosgene⁵ or nitrogen dioxide.⁷

While investigating the effects of prolonged exposure of rats to increased oxygen partial pressures, we observed bullous changes in the lungs of most of our animals.³ It was felt that the detailed study of this phenomenon in experimental animals may have direct bearing on bullous formation and emphysema as it occurs in man because anatomically it did resemble bullous emphysema in humans. We also expanded these studies to larger animals (dogs) in an attempt to delineate more clearly the changes in pulmonary circulation and structure of the lung during the development of our "experimental bullous emphysema."

In these studies we have taken into account the sometimes wide difference of opinion about what constitutes emphysema. The criteria of the disease depend at times upon whether emphysema is viewed by a clinician or by a pathologist. In general, however, a definition of emphysema includes:

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Presented before the Section on Pathology at the 96th Annual Session of the California Medical Association, Los Angeles, April 15 to 19, 1967.

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(1) physiologic evidence of increased airway resistance (and its byproducts, such as expiratory slowing and decreased maximum voluntary ventilation); (2) changes in compliance or elastic characteristics of the lung; (3) radiographic appearance of changes in lung density; (4) changes in pulmonary circulation and perfusion of the lung; and (5) where possible, pathologic examination and evidence for airway obstruction, alveolar distension and rupture and the gross appearance of bullae. We have discussed the preliminary findings from these studies for the first two criteria in a previous paper.¹ The present paper details our findings for the last three items.

These studies should be of concern for those interested in the clinical pathogenesis of emphysema and may serve as a model for future study of chronic obstructive diseases. It is also of prime importance to point out that these bullous changes in animals are the result of prolonged exposure to a high partial pressure of oxygen. These findings may have clinical importance since there is an ever-expanding use of high concentrations of oxygen as acute or chronic therapy for cardiopulmonary disease and in the field of hyperbaric medicine.

Methods

One hundred male Sprague-Dawley rats weighing 100 gm (four weeks old) were divided into five groups and exposed to 100 per cent oxygen at ambient pressure for up to five weeks. Rats of this size were chosen after they had previously been shown³ to resist the pulmonary response usually associated with oxygen breathing and resulting in death within three to four days. The exposure system for small animals has been previously described.⁴

One group of rats was removed from the exposure chambers and sacrificed weekly. The lungs were immediately removed, inflated with formalin at a constant pressure of 5 cm of water and subsequently prepared for histological examination. Two of the animals from each group were used for microradiography of the pulmonary circulation after the method of Quigley and coworkers.¹⁴

The dog study consisted in exposing ten purebred beagles to 60 per cent oxygen at ambient pressure for 33 days. For this, a large walk-in altitude chamber with a complete environmental control and monitoring system was used. Two of the dogs were sacrificed at weekly intervals during

the study; six of them had dyspnea and pronounced respiratory effort when killed. An identical technique was used in lung tissue preparation in both studies, except the dog lungs were inflated with formalin at pressures between 8 and 10 cm (water).

Before the study began, in four of the dogs the pulmonary artery was catheterized by way of the external jugular vein. This catheter was then left as a chronic preparation for pulmonary angiography for the duration of the experiment. Pulmonary angiography was performed weekly on these animals and on a control dog with a chronic pulmonary artery catheter, but exposed to air for the duration of the experiment.

In both cases, equal numbers of control animals were exposed to ambient air, sacrificed, and treated the same as the experimental animals. In the exposure chamber, the temperature was maintained between 68 and 72°F, relative humidity between 40 and 60 per cent, and carbon dioxide below 1 per cent.

Results

Histological study of the lung tissue removed from the animals during the first two weeks of exposure revealed focal hemorrhages and widespread pulmonary edema. There were wide full areas of edema around the vascular structures. The lung parenchyma had been pushed aside and the areas of edema were frequently infiltrated by scattered lymphocytes and occasional eosinophilic leukocytes. These are the changes usually associated with the pulmonary oxygen toxicity syndrome. The alveoli and tracheobronchial tree appeared undamaged.

Of interest, however, was that after two to three weeks of exposure the perivascular edema diminished and these areas began showing signs of organization, with the invasion of small capillary vascular channels and an increased infiltration of lymphocytes. Grossly, bullae were observed on the surface of the lungs at about three weeks.

At the end of four weeks, the perivascular edema had literally disappeared. Many of the alveolar septa were ruptured, bullae were prominent throughout the lungs, and in addition, lesions appeared in the bronchi. The bronchi showed a great increase in the number of goblet cells, which were filled with a mucinous material. There was hyperplasia and some metaplasia of the epithelial cells lining the terminal bronchioles, and even in

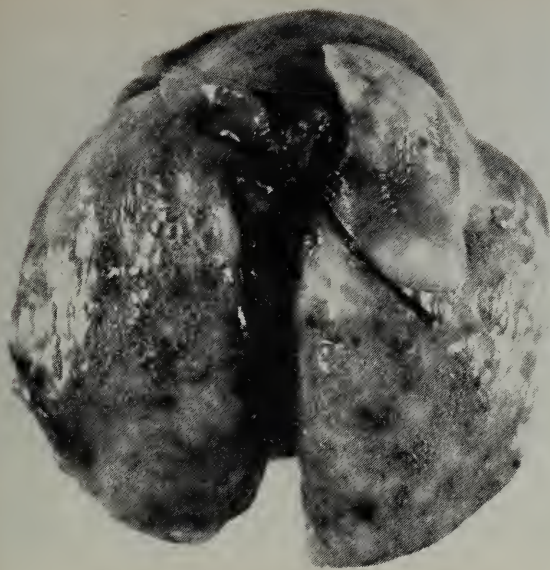


Figure 1.—Whole rat lung exposed to 100 per cent oxygen at 760 mm of mercury for four weeks. The lung appears grossly emphysematous and shows gross bullae.

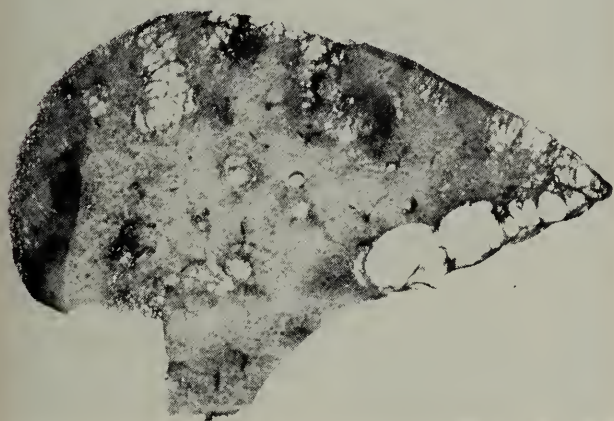


Figure 2.—Longitudinal section of rat lung exposed to 100 per cent oxygen at 760 mm of mercury for five weeks. The lung was fixed by inflation with air bubbled through formalin and maintained at 5 cm (water) pressure. Note the extensive bullae formation throughout the lung. Section is approximately 3 mm thick.

this area, goblet cells had begun to appear. Goblet cells were not observed in the bronchi of any of the control animals, and the appearance of these cells has been described by others⁷ to coincide with the appearance of emphysema.

By five weeks, cellular exfoliation had also occurred in the terminal bronchi, and the alveolar ducts were frequently well filled with cellular debris. All the lungs were large, pale, foamy, grossly overinflated and covered with extensive bullae (Figures 1 and 2).

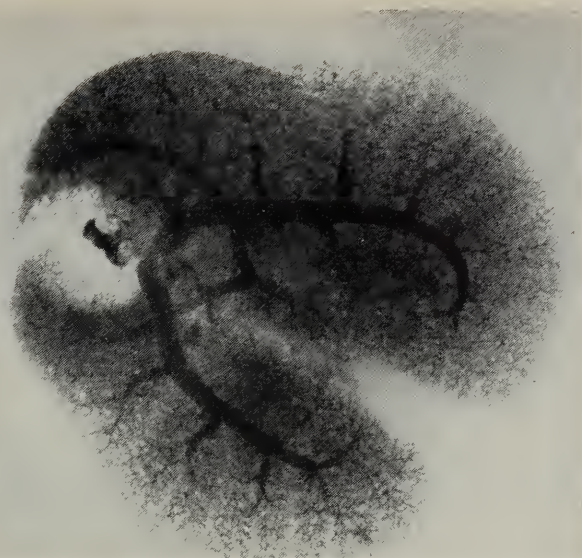


Figure 3.—Macroradiograph of normal rat lung. The lung was injected through pulmonary artery with Micropaque® injected at a pressure of 26.0 mm of water. (Magnification 9X.)

Macroradiographic studies indicated progressive changes and by four weeks the pulmonary artery and its main branches were enlarged and tortuous. The intrasegmental branches were prominent and enlarged, and extended into the periphery of the lung. The arteriolar bed was absent or reduced, particularly in the most decidedly affected lungs (Figures 3, 4, 5 and 6).

Pulmonary angiograms revealed progressive development of a pulmonary artery hypertension and hypertrophy. The enlargement of the pulmonary artery started between one and two weeks in the dogs. In one dog, for example (Figure 7), the diameter of the right pulmonary artery at its origin increased from 0.8 cm before the study to 1.9 cm after four weeks of exposure to oxygen. Post-mortem examination of the heart revealed a two-fold to three-fold increase in the right ventricular size in all the oxygen-exposed dogs. Hemodynamic measurements confirmed the angiographic evidence of pulmonary hypertension developing after the onset of oxygen exposure. These findings consisted of increased pulmonary artery pressures, decreased cardiac output and increased pulmonary vascular resistance. These results will be published in a subsequent report.²

Discussion

The question of duration and tolerable exposure to increased oxygen tension, either for medical or aviation purposes, remains to be answered. From our studies, it appears that the prolonged pulmo-



Figure 4.—Macroradiograph of rat lung after exposure to 100 per cent oxygen at 760 mm (mercury) for five weeks. The lung was injected through pulmonary artery with Micropaque® at 26.0 mm of water. Pulmonary artery and main branches are enlarged and few arterioles are present. (Magnification 8.5×.)



Figure 5.—High magnification (×20) of periphery of normal lung in Figure 3. The fine structure of arterioles is clearly visible.

nary irritation induced by a chronic inhalation of oxygen at high pressure may lead to a condition which morphologically resembles bullous emphysema in man.

The mechanism behind the "bullous emphysema" we brought about is speculative, but several clues do exist. A primary lesion after the inhalation of oxygen or other agents which have recently been used^{5,7} to produce emphysema-like syndromes, has been caused by vascular changes characterized initially by hemorrhage, edema and then subsequently emphysematous changes. The emphysematous changes, however, have also been noticed to appear simultaneously with the vascular damage. While it is recognized that the progression

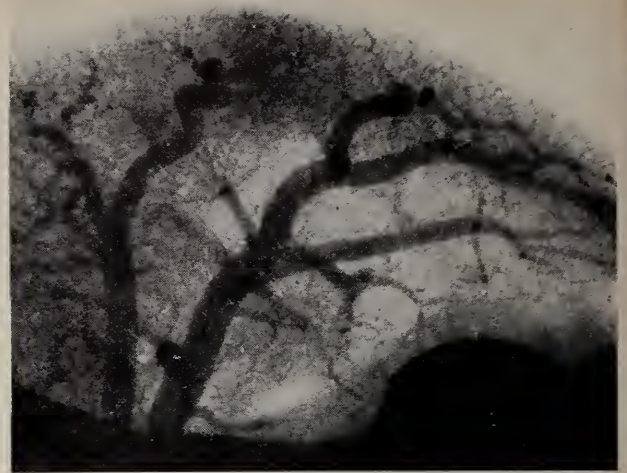


Figure 6.—High magnification (×20) of periphery of lung in Figure 4. The large branches of arteries extend to edge of lung and the vessels appear enlarged and tortuous. Few arterioles are present.

of emphysema is not a simple process but a very complex one dependent upon several factors, our studies suggest that perhaps the major underlying cause of the bullous disease may well be the vascular changes associated with the first weeks of breathing of oxygen under pressure. Added support is given by the decided change in the vascular bed during the third and fourth weeks when the alveolar and airway changes began to appear.

The vascular changes that we observed have been recognized as typical of human emphysema.^{9,10} However, opinion as to the relationship between these changes and the pathogenesis of emphysema is at wide variance among investigators. Liebow¹¹ and Heppleston⁹ contend that changes in vascularity are secondary manifestations and do not constitute the essential basis of emphysema. This essential basis, they feel, is a deficiency of muscle in the bronchial tree or possible abnormalities of the thoracic cage leading to fixation of the thorax in a position of partial inspiration. McLean¹² is of the opinion that the basic lesion in emphysema is in the bronchiole and that the breakdown of tissue distally is due to airtrapping resulting from the bronchiolar failure. Strawbridge's¹³ review supports our findings. He also produced a high incidence of emphysema in rabbits by injecting Caledon blue dye¹⁶ which tended to aggregate in the precapillaries and capillaries. This technique produced vascular obstruction in the lungs, and he suggested that the resultant obstruction and ischemia played a prominent role in the development of emphysema.

In our study the possible importance of vascular

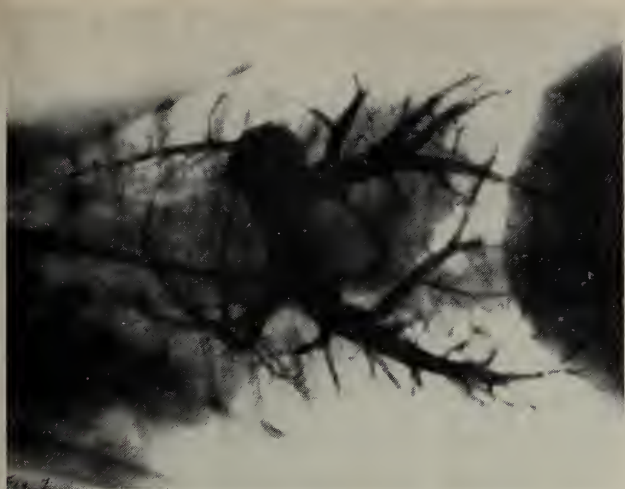


Figure 7.—Pulmonary angiogram of dog exposed to 60 per cent oxygen at 760 mm (mercury) for four weeks. The pulmonary artery is grossly enlarged. Seventy-five per cent Hypaque® injected at 300 pounds per square inch.

obstruction in the genesis of bullous disease is further emphasized by the hypertension in the dogs, indicative of an increased pulmonary vascular resistance and probable ischemia. This hypertension may be related to the increased vascular resistance West¹⁷ showed to result from perivascular edema. However, while our studies do suggest the paramount importance of the vascular response, terminal airway obstruction as a causal and strong contributing agent cannot be discarded. The pronounced exfoliation in the airways of the bullous lungs in the present study cannot preclude the possibility that this obstruction causes the distal alveolar damage.

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Complications Following Ingestion of LSD

In a Lower Class Population

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■ *A study was made of 49 patients observed at Los Angeles County Hospital as a direct result of LSD ingestion. In 57 per cent of these patients an extended psychosis developed although they had no previous history of psychotic behavior. The patients were young and of low socio-economic order. Those who were discharged from the County Hospital made poor social adjustment in succeeding months.*

REPORTS DESCRIBING complications due to ingestion of LSD-25 (d-lysergic acid diethylamide) have been appearing more frequently in the medical literature in the past few years.^{1-3,7,8}

Early in 1966 it was noted that increasing numbers of patients with symptoms that could be related to use of LSD were being seen in the Psychiatric Evaluating Area and Inpatient Service of the Los Angeles County Hospital. It was therefore decided to study in greater detail all patients whose problem when they were first examined was related to the use of LSD. This report concerns our experience with such patients during a three month period in 1966, from April through June.

There was no selection made in admitting the patients. No effort was made to encourage admission of these patients, as this would be against the current policy of avoiding unnecessary hospitalization. Patients were admitted only if the psychopathology was so severe that care in hospital was the treatment of choice or other appropriate treatment was not available. Only after the patient was admitted was he evaluated for the purpose of this study.

As part of the study, each patient was interviewed in an attempt to elicit data regarding symptoms, ethnic and socio-economic background, drug dosage, frequency of use and self-administration of adjuvant drugs. When possible, the Bender-Gestalt and Minnesota Multiphasic Personality Inventory (M.M.P.I.) tests were administered.

Characteristics of Study Group

During this three month period 49 patients, 37 male and 12 female, were admitted to the Psychiatric Inpatient Service of the Los Angeles County General Hospital because of complications following ingestion of LSD. There were 43 Caucasians (88 per cent of total patient group), five Negroes (10 per cent) and one of Mexican-American origin. The general admission rates to the Psychiatric Unit show 17 per cent of the patients to be Negroes. As shown in Table 1, the majority of the patients were under 25 years of age. Since most patients admitted to the Los Angeles County General Hospital are primarily from the lower socio-economic groups, the number of admissions suggests that the use of LSD is becoming a problem for these groups. Eighty per cent of the patients in the group studied were in the lower socio-economic classes, using Hollingshead and Redlich's criteria.⁵ The educational background for the group is shown in Table 2.

It was difficult to document drug dosage, as information depended upon the subjective descriptions and memory of the patients. The product used also was not necessarily pure, since it was obtained illicitly. Nevertheless, the reported dosage of LSD varied from 100 micrograms to 2,000 micrograms. The onset of symptoms varied from the day of ingestion to an onset as late as three months after the last dose of LSD.

Each patient was questioned about the concurrent use of other drugs which might have been related to the development of psychiatric symptoms.

Submitted 30 March 1967.

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TABLE 1.—*Age of Patients in Group Studied*

| | No. of Patients | % of Total Group |
|-------------------------|-----------------|------------------|
| Less than 18 years..... | 2 | 4 |
| 18-25 years..... | 39 | 80 |
| 25-35 years..... | 6 | 12 |
| More than 35 years..... | 2 | 4 |

TABLE 2.—*Educational Background of Patients*

| No. of Years in School | No. of Patients | % of Total Group |
|-------------------------|-----------------|------------------|
| Less than 12 years..... | 16 | 32 |
| 12 years..... | 15 | 30 |
| 12-16 years..... | 17 | 34 |
| More than 16 years..... | 34 | 6 |

TABLE 3.—*Kinds of Complications Resulting from Use of LSD (According to Classification Developed by Frosch and coworkers)*

| | No. of Patients | % of Total Group |
|------------------------------|-----------------|------------------|
| Acute Panic Reactions..... | 15 | 30 |
| Reappearance of Symptoms.... | 6 | 12 |
| Extended Psychosis..... | 28 | 57 |
| TOTAL..... | 49 patients | |

It was found that most of our patients had taken other drugs as well as LSD. The drugs taken included the amphetamines, marijuana and heroin. It was difficult to document any cumulative effect, as these drugs were not consistently taken with LSD.

Psychological Testing

Psychological testing was attempted as soon as the patients were able to cooperate, which was usually about the third hospital day. In the first 48 hours the patients were much too disturbed or suspicious, often to the point of requiring seclusion. After the initial panic reaction had subsided, the patients were given the Bender-Gestalt test and the M.M.P.I.

The Bender-Gestalt test was scored quantitatively according to the method devised by Pascal and Suttell. The results were within normal limits in the majority of our LSD cases, whereas the same test when administered to a control group of young schizophrenic patients was abnormal in 50 per cent of the cases. The Bender-Gestalt test can serve as an index for perceptual-motor function, and thus tends to be abnormal in cerebral damage and in psychosis.

The M.M.P.I. was scored in our cases and the results showed a pattern which was similar to the pattern seen in young schizophrenic cases.⁴ This was confirmed by administering this test to a control of young schizophrenic patients.

Thus, the psychological tests administered to our

LSD patient group were very similar to the pattern seen in schizophrenic patients, but could be differentiated by the results of the Bender-Gestalt test.

Results of Study

In 1965 Frosch and coworkers³ described three types of syndromes into which most patients with complications from ingestion of LSD could be classified. They were as follows: panic reactions, reappearance of drug symptoms without reingestion of the drug, and overt psychosis. The present group of 49 patients could be classified as shown in Table 3.

Acute Panic Reactions

Acute panic reactions were seen at first in all the patients. This was an acute anxiety reaction in which the patients essentially relived the horrors they experienced during the psychedelic experience. During this period, the patients usually needed large doses of phenothiazines and often needed to be secluded as well. The acute panic reaction lasted a few days, and if the patient seemed to recover completely after this, he was considered to have had only an acute panic reaction. Other patients remained in this state, which then could not be differentiated from psychosis. Patients in a panic state often became quite paranoid, and the paranoid delusions were often expressed as fears of homosexual attack.

About one-third of the patients studied had an acute panic reaction severe enough to necessitate care in hospital.

Reappearance of Symptoms

In some patients the LSD experience reoccurred, including the visual illusions and hallucinations, without further ingestion of the drug. Patients would say that a particular light or sound would remind them of the total LSD "trip," and they re-lived the entire psychedelic experience. One patient could, by looking at a lamp at a particular angle, recall and re-live his entire LSD experience at will. These patients are similar to the ones described by Rosenthal,⁷ who prefers the term *hallucinosis*. Rosenthal postulated some damage in the neuro-optic tracts as the cause of this phenomenon.

Extended Psychosis

In some patients the symptoms extended beyond the acute panic reaction and became almost indistinguishable from the manifestations of acute schizophrenia. The majority of these patients

stayed at the Los Angeles County Hospital for about 10 days and then were committed to a state hospital for further care. In about two-thirds of the patients in the study, extended psychosis developed, presumably as a result of their LSD experience.

Follow-up

An attempt was made to evaluate patients in the community after their discharge from the hospital. Patients committed to a state mental hospital were excluded. Seventeen patients were interviewed in the community, anywhere from one to five months after discharge from this hospital. We were particularly interested in whether or not they were working, in the extent of their social intercourse and in continued drug usage. It was found that the majority of those interviewed were functioning marginally in the community. Often, they were not working or were working only part-time. The degree of socialization also was very minimal. Often the patients lived alone and had contact only with a few friends. Very few of those interviewed had used LSD since discharge from the hospital, but many continued to use other drugs. Most of the patients interviewed were afraid of continued LSD usage because of their bad experience.

Discussion

The data obtained in the present study substantiate the occurrence of a very serious psychiatric disturbance due to the ingestion of LSD. Two-thirds of the patients went into an extended psychosis which could not be differentiated from schizophrenia, and a follow-up study of the remaining third showed a patient population only minimally functioning in the community.

A number of factors may be uncovered in determining the seriousness of the outcome. First of all, the question arises as to the pre-morbid personality of the patients. Were these patients functioning at a borderline psychotic level before they took LSD? If so, then the LSD may have triggered a latent psychosis. If, on the other hand, this was a basically healthy population, it may be assumed that LSD caused the psychosis. Unfortunately, our data cannot decide this issue completely as very little is known about the pre-morbid personality. However, it must be borne in mind that none of the patients had had previous admission to hospital for psychiatric disorder. Psychological tests produced some interesting results. There seemed to be some difference in the results

obtained on the Bender-Gestalt test in our patient population as compared with a similar group of patients diagnosed as being schizophrenic. The latter group of patients tended to have abnormal Bender-Gestalt tests, while the group of patients put in hospital because of serious complications from LSD ingestion tended to have normal Bender-Gestalt tests. Abnormal Bender-Gestalt tests have been reported before in schizophrenic patients.⁶ The normality of this test in our LSD group suggests no persistent perceptual motor defect produced by LSD, measurable by the Bender-Gestalt test. If there is brain damage due to LSD, as has been postulated,⁷ more definite data should be produced.

Other factors which may have influenced the seriousness of the outcome, are the relatively high drug dosages used, the purity or impurity of the LSD used, and possibly the use of adjuvant drugs such as the amphetamines.

The data presented here also indicate that the use of LSD may be becoming more prevalent in the lower socio-economic classes. It has previously been shown that schizophrenia severe enough to cause hospitalization of the patient tends to be more prevalent in the lower socio-economic classes. This may be due to lack of community support, to family disorganization or to unknown factors. All these factors were present in our patients, who were mostly from the same social class. This suggests that the ingestion of LSD by a patient from the lower socio-economic class may add a more potent psychic stress to an already susceptible person.

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Clinical Experiences with Jejunal Interposition for Postgastrectomy Syndrome

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■ *Remedial operation for intractable postgastrectomy syndrome utilizing an isoperistaltic jejunal segment interposed between the gastric remnant and duodenum has been highly successful in the hands of European surgeons. This secondary operation is rarely performed in this country.*

The author reports his experience with three patients. The initial results were uniformly excellent. In time, some symptoms recurred in two patients.

SERIOUS POSTGASTRECTOMY COMPLAINTS are generally transient and may be satisfactorily controlled or alleviated by diet, medication and time.

Rarely, postgastrectomy distress is both permanent and ravaging.

One seldom sees more miserable or constantly suffering patients. They are wasted, listless and endlessly sick. They cannot eat or work or play, and their unending unsuccessful search for help adds untold mental discouragement to their already debilitating physical complaints. They lose hope as well as weight and their enjoyment and interest in life slips away. They become a burden to themselves and their families. Dependent, unproductive and unhappy, they are ambulatory invalids well described in the phrase "gastric cripple."

In times past, such patients have often been accepted as irretrievable medical and surgical

failures and, like the rearguard battalion in a hopeless military engagement, they have been "written off."

Many, however, may be aided by careful application of one of the several remedial operations currently fully developed and in wide use (Figure 1). My personal preference among these surprisingly various and ingenious choices has been the operation devised by Henley and developed by Hedenstedt.^{2,4,5} It has the great virtue of simplicity as well as reported effectiveness.^{2,4,5,6} Its basic feature is the interposition of an unreversed isoperistaltic segment of jejunum between the gastric pouch and duodenum. European surgeons have been quite happy with the procedure, used both primarily at the time of gastric resection and secondarily for the correction of the dumping syndrome.^{2,3,4,5,6} The operation has been used but rarely in this country and only scattered reports are available for study.^{7,12,15,16} My own experience with three patients is reported below.

CASE 1. A 45-year-old man was admitted to hospital with complaint of bilious vomiting, pain

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Presented before the Section on General Surgery at the 96th Annual Session of the California Medical Association, Los Angeles, 15 to 19 April 1967.

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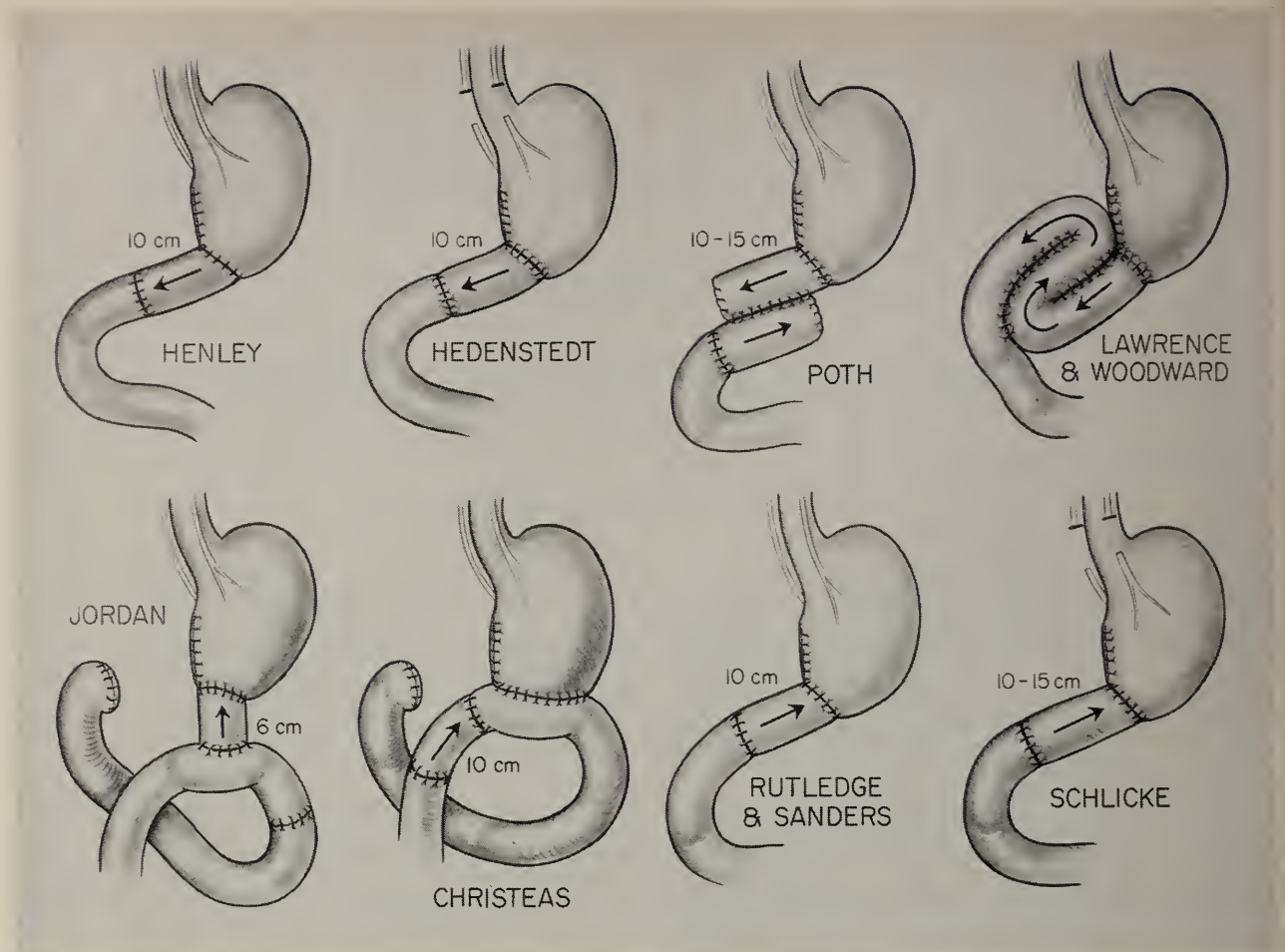


Figure 1.—The many diverse ways in which small bowel segments may be utilized in remedial gastric operations are depicted. (Adapted from Herrington, J. L., Jr.)

during and after meals and symptoms suggestive of the early postprandial dumping syndrome.

Eleven years previously, a radical subtotal gastrectomy with Billroth II anastomosis had been performed. Years of duodenal ulcer troubles had been replaced by years of postgastrectomy troubles. Meals produced unpleasant effects and were often avoided. Weight loss totaled over 50 pounds.

X-ray films after a barium meal (Figure 2) showed a very small gastric remnant. The contrast material poured into the afferent loop, churned about there for several minutes and ultimately spilled over into the efferent side. Severe, cramping abdominal pain coincided with these events. The small bowel transit time was not shortened. Absorption studies and a challenging glucose meal produced equivocal findings.

CASE 2. A 46-year-old man was admitted with complaint of inability to eat, severe postprandial nausea and pain, and intermittent diarrhea. These symptoms had begun insidiously some 30 months

after subtotal gastrectomy with Billroth II anastomosis for intractable duodenal ulcer disease. They persisted unabated through the six years up to the time of admission to hospital. Weight loss totaled 65 pounds.

Barium meal studies (Figure 3) showed a small gastric remnant with speedy unimpeded filling of both afferent and efferent loops. The small bowel transit time was normal. Fecal fat excretion studies demonstrated borderline steatorrhea (8.5 gm in 24 hrs).

CASE 3.* A woman 38 years of age was seen six years following vagotomy and subtotal gastric resection with Billroth II anastomosis (Figure 4). Pain and epigastric fullness occurred during and after meals. As these complaints were aggravated by a large meal, the patient ate often and a little at a time. Diarrhea was a constant and very serious problem. She had from six to as many as 40 stools daily. Nothing gave her relief. She was extraor-

*Included in this series through the courtesy of Benjamin J. Feldman, M.D.



Figure 2.—(Case 1) Preoperative film showing tiny gastric pouch (arrow) and preferential filling of the afferent loop.



Figure 3.—(Case 2) Preoperative film demonstrates rapid filling of afferent and efferent loops.

dinarily cachectic and frail, weighing 69 pounds at the time of examination.

Operation

An identical corrective operation was performed in each of the three patients. This was the operation of Henley, the isoperistaltic jejunal interpo-



Figure 4.—(Case 3) Preoperative film. The gastric remnant is small, empties rapidly and the barium speeds along the small intestine.

sition between stomach remnant and duodenum. The technique is illustrated in Figure 5. As can be seen, the efferent limb of the previously made gastrojejunal anastomosis can be conveniently fashioned for the interposition without disturbing the anastomosis itself, save for closure of the afferent aspect.

End-to-side jejuno-duodenal implantation for the interposed segment was preferred over end-to-end suture in the hope (not realized) that the former might act functionally in a valve-like manner and perhaps simulate the lost pyloric sphincter.

The operative procedure was both easily accomplished and well tolerated. In two patients a return to "normal" diet was delayed for two weeks, apparently because of initially sluggish peristalsis in the transposed jejunal segment.

Results

The early results in all three patients were uniformly excellent. All major complaints completely disappeared. Early return to a normal unrestricted diet was accompanied by a rapid and impressive gain in weight.

The first patient declared himself vastly improved and gained 15 pounds in six months. He still felt more comfortable with smaller and more frequent meals than the conventional three a day but he seemed well satisfied.

The second patient had a weight gain of 35

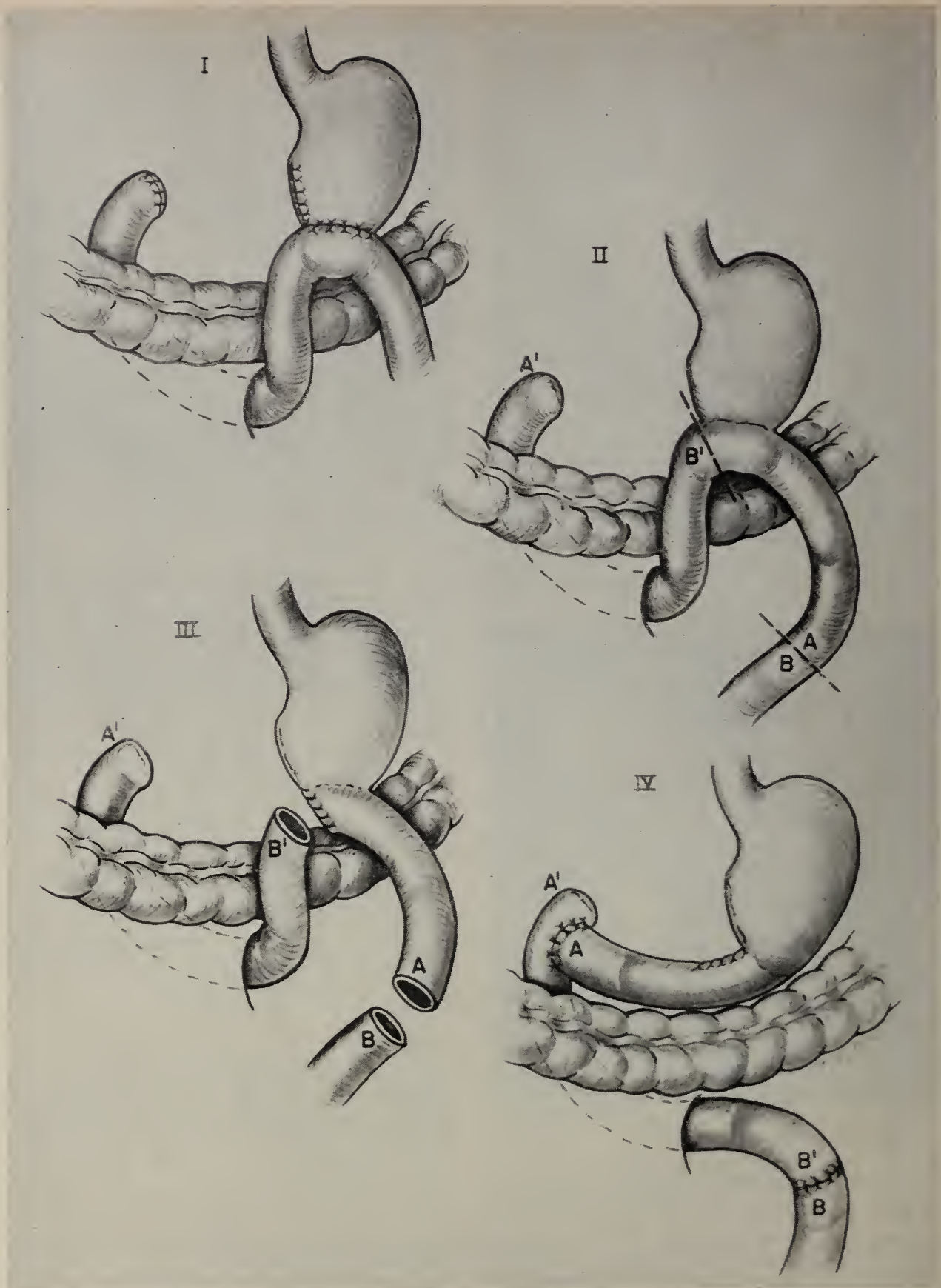


Figure 5.—I. The operative field before reconstruction. II. Dotted lines indicate sites of transection of the afferent and efferent loops. III. The divisions have been made and the afferent aspect of the gastro-jejunosomy closed. IV. The completed operation.

pounds in three months. He was eating anything and everything without difficulty. Diarrhea had ceased and the fecal fat excretion dropped to well within normal limits.

The fulminating explosive diarrhea in the third patient subsided gradually and stopped completely a few weeks after operation. Three normal pain-free meals were taken with pleasure and the patient slowly and steadily gained weight.

Unfortunately, the initial superb effects of operation have not been maintained in the first two patients. After a peak weight gain and symptom-free period of six and three months, respectively, some of the preoperative distress returned. Although the troubles are much milder than before, both patients state their symptoms are enough to again interfere with eating. Some of the early gain in weight has ebbed away. The weight stabilized at 7 pounds above the preoperative level after two years in Case 1, and at plus 22 pounds in seven months in Case 2. Both patients are unquestionably improved; indeed, one is planning to work again for the first time in five years. However, some symptoms remain and both patients are visibly disappointed at an imperfect long-term result.

The initial excellent result has been sustained in Case 3. In one year the patient has gained 15 pounds, is symptom-free and is entirely and enthusiastically pleased with the effects of the operation.

Discussion

There is more to postgastrectomy distress than the serious vasomotor complex of classic dumping. The "small stomach" and afferent loop syndromes (bilious vomiting) are examples of other clearly recognized components. These various abnormalities may be present singly or in combination in any individual patient, and one or another may predominate in unpredictable fashion. The accompanying weight loss, malnutrition and anemia are simply heirs of a decreased caloric intake. Eating becomes a painful rather than a pleasurable necessity.

It is important to recognize what part or parts of the postgastrectomy syndrome complex one is dealing with in any specific case. Proper selection of patients for operation is as important here as it is for other surgical procedures. A patient with pure "small stomach" syndrome requires an opera-

tion designed to create a reservoir to replace the lost stomach.^{9,11} Bilious vomiting is easily corrected by elimination of the afferent loop.¹⁷

The vasomotor complex, diarrhea and postprandial pain are problems not so simply explained or solved. This is a dark area and the picture is confused and mysterious.

The entire symptom complex or aggregate of "syndromes" is best explained by the concept of rapid "dumping" of food into the adjacent small intestine. This is true whether the anastomosis is a Billroth I or Billroth II or gastroenterostomy or pyloroplasty. In each instance the pylorus is destroyed and a patulous sphincterless stoma purposefully created. The food bolus pours into and overwhelms the unprepared gut, filling and distending it. Perhaps the accompanying colicky pain or "intestinal hurry" are an understandable if unfortunate intestinal response. The smallness of the stomach itself may contribute to rapid filling of the gut; it will only hold so much, and of necessity the food bolus races through the open passageway.

Recognition of these many variables and correctly placing them in relative importance in a specific clinical situation are the key to uniform rather than scattered success in surgical procedures to alleviate postgastrectomy syndromes.

The isoperistaltic jejunal interposition of Henley-Hedenstedt is very appealing because of its workable simplicity. The mixed and contradictory results with its infrequent use in this country are puzzling, particularly when contrasted to the high rate of success reported from Europe in hundreds of cases.⁶

Perhaps the plicated pouches of Woodward¹⁷ and Lawrence⁹ or the double pouch of Poth¹¹ have a higher rate of complete success. I am not certain of this. I do know they are difficult and tedious to construct in the laboratory. In fact, when animals are "prepared" for a remedial operation by previous partial gastrectomy and profound malnutrition and diarrhea are established, the fashioning of the complex plicated pouches at a subsequent operation is not tolerated. The animals die, apparently unable to withstand the ordeal of radical gastrectomy and the long complicated construction of the secondary pouch.¹⁰ Isoperistaltic jejunal interposition, on the other hand, is well tolerated in those circumstances. The results in a series of pilot experiments are impressively good. The animals gain weight rapidly following jejunal interposition and are soon restored to health and vigor,

at times as early as four weeks after secondary operation.¹⁰

Whether to place the interposed jejunal segment in the unreversed (isoperistaltic) or reversed (antiperistaltic) position is a widely debated and unsettled point. Some good clinical results with reversed segments have been reported.^{6,8,12,13,14} Stemmer and Connolly¹⁴ used the reversed segment in a highly original manner. They treated three patients who had severe dumping after vagotomy and pyloroplasty. A short reversed segment was interposed between the intact stomach and duodenum and excellent results were achieved.

Rutledge¹² and Farris,¹ however, indicated that real problems with obstruction may develop, and the operation is prone to late failure.

My experience in managing the three cases reported herein raises important questions about the isoperistaltic interposition operation. Why did the early fine result in the first two patients deteriorate into the "fair" category, and why does the third patient, in contrast, continue to do extremely well?

Perhaps the first two patients were not good candidates for any sort of remedial operation. A seldom discussed aspect of the overall problem is that of "psychic overlay." Both patients had it in full measure. This is indefinable and difficult to assess, but it may well be as important in success or failure as the host of data that may be accumu-

lated and subjected to precise scientific analysis. No such problems were present in the third case, and the result remains excellent.

A few comments as to why the operation should work at all are in order. It seems that the effectiveness of all the various remedial operations depends upon the creation, in a roundabout fashion, of a substitute pylorus. This is true whether one plicates or reverses or does not reverse the interposed segment. The "new" stomach no longer "dumps"; it empties "rhythmically and in installments."³

The isoperistaltic segment does not act as a reservoir. This point is clear. But the stomach does empty its contents in installments, and more slowly than before (Figures 6 and 7). Somewhat unexpectedly, I found the "hangup" at the gastro-jejunal anastomosis rather than at the site of jejuno-duodenostomy. Although some barium would pool in the interposed segment for a short moment, for the most part it moved right on through and the segment acted as a simple conduit (Figures 6 and 7).

Why the undisturbed gastrojejunostomy stoma should "dump" in the Billroth II position and not do so, at least to the same extent, in its transposed position is an intriguing question. The answer may be very simple. Perhaps it is the altered gastro-jejunal angle, or the new "hanging" position, or even the pull of gravity, that makes the

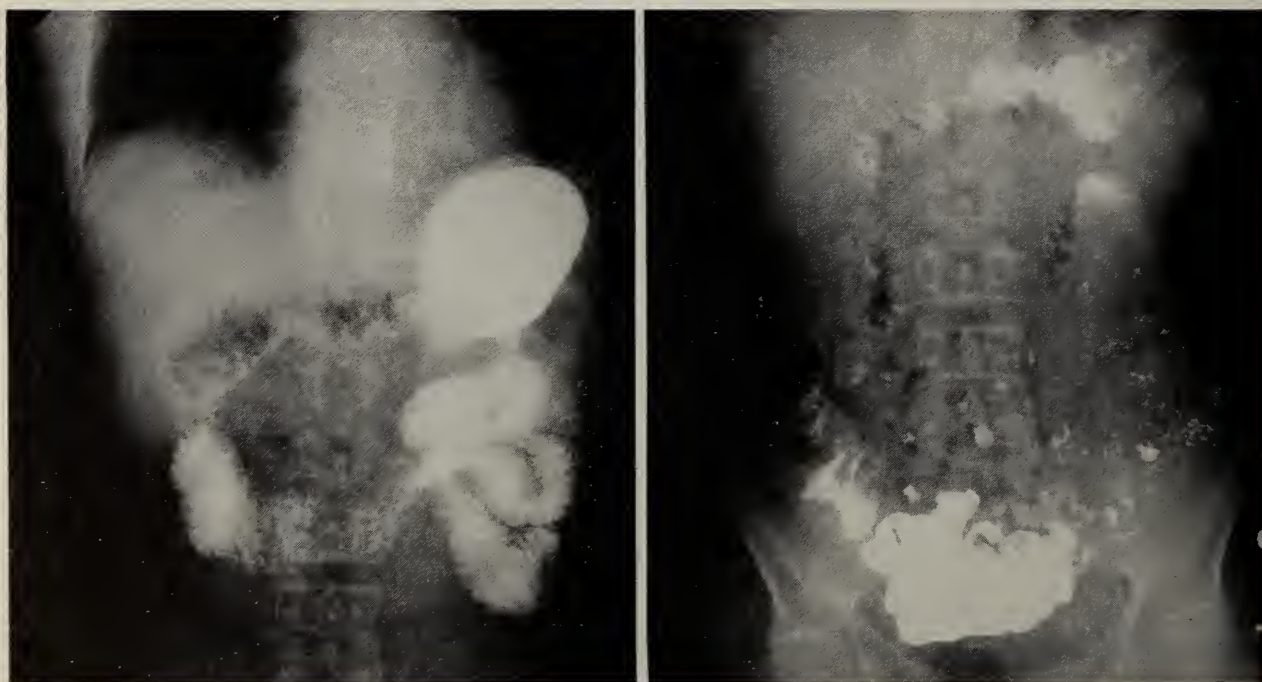


Figure 6.—(Case 2) *Left*, barium fills the gastric remnant and moves into the gut "rhythmically and in installments." *Right*, three-hour film seven months after operation. Barium outlines the interposed jejunal segment and a small quantity remains in the stomach.

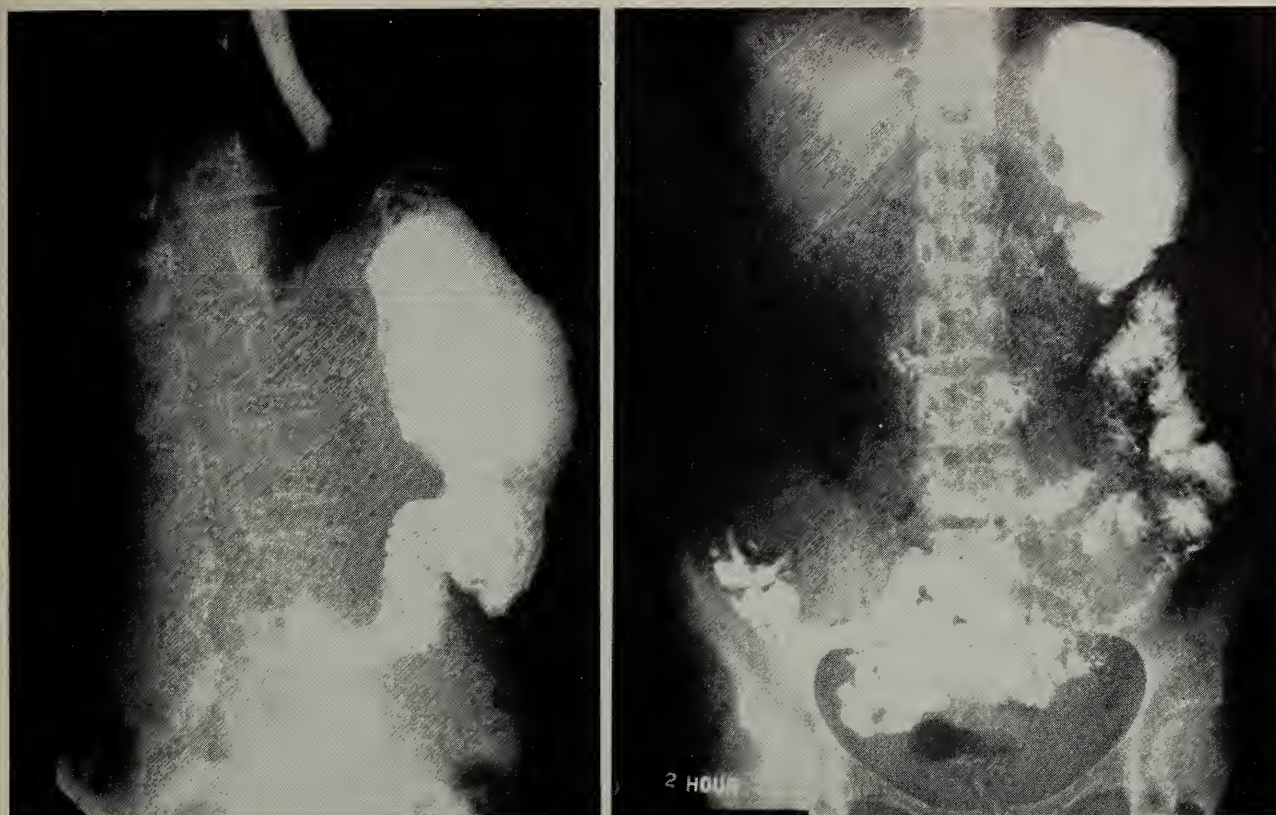


Figure 7.—(Case 3) *Left*, the interposed segment conducts barium to the duodenum. *Right*, the two-hour film shows much barium remains in the stomach, demonstrating gradual gastric emptying in "installments."

difference.

Fluoroscopic observation of the interposition in the early and late postoperative periods in Case 2 suggested that gastric emptying speeds up again in time. The jejunal conduit was decidedly sluggish at first, but later it recovered its activity. The symptoms in Case 2 returned in part coincident with this discovery.

The proper place of the isoperistaltic jejunal interposition (Henley) in reconstructive operation for postgastrectomy distress is unsettled at this time. The results are good enough, however, to warrant further clinical trial in properly selected cases.

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The Current Application of Maximal Treadmill Stress Testing

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■ *Treadmill stress testing has many applications in the overall evaluation of ischemic heart disease, both as a diagnostic aid and as an aid in serially following patients under study. Its use in the evaluation of procedures designed to improve myocardial function and coronary perfusion is of great value, for it can supply objective evidence without recourse to more difficult procedures such as determination of blood lactate levels. Ancillary procedures which may complement treadmill stress testing may prove to be valuable additions to the study of ischemic heart disease.*

The reported high rate of false-positive Master two-step tests would tend to make the treadmill exercise test more attractive.

SINCE THE EARLY STUDIES by Master,¹⁰ utilizing a simple two-step exercise test to evaluate the patient's pulse response to mild stress, there has evolved a more sophisticated method for determining a given patient's tolerance to exercise and a means of evaluating the physiological parameters. The use of a treadmill for such testing was a natural evolution since the conditions lacking in the so-called two-step test (namely a constant work load which may be graded at various time intervals, a more constant and accurate monitoring system, and evaluation of several physiological responses to steady-state exercise) are easily included. The reproducibility, simplicity and safety of treadmill stress testing is borne out by our statistics of evaluating more than a thousand patients by this means without serious complication of morbidity or mortality. Almost all age groups may be studied by maximal stress testing and there are few absolute

contraindications.

Physiological responses to exercise may be studied and correlated with predictive values of laboratory normals. Since the heart extracts the maximum amount of oxygen from the coronary artery blood with the patient at rest, the coronary flow can be considered linear in relation to cardiac work.¹⁰ When the work of the body increases, the cardiac output and thus coronary flow increases in a reliable, predictable ratio.¹¹ The stroke volume does not increase as much as work increases⁴ and therefore the pulse rate turns out to be a reliable guide to relative cardiac output in most circumstances. Since we increase the work of the heart in a stepwise fashion, the pulse rate will increase until the peak cardiac output is attained. This produces a predictable pulse response for each age group regardless of strength or conditioning.^{1,5} Thus a man of age 40 has a predicted peak pulse rate of 180 and how much work he does to reach this pulse is a matter of strength and conditioning (Chart 1). A fat and flabby patient may reach a pulse of 180 in 3 minutes of exercising at 1.7 MPH on a 10 per cent

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Submitted 24 May 1967.

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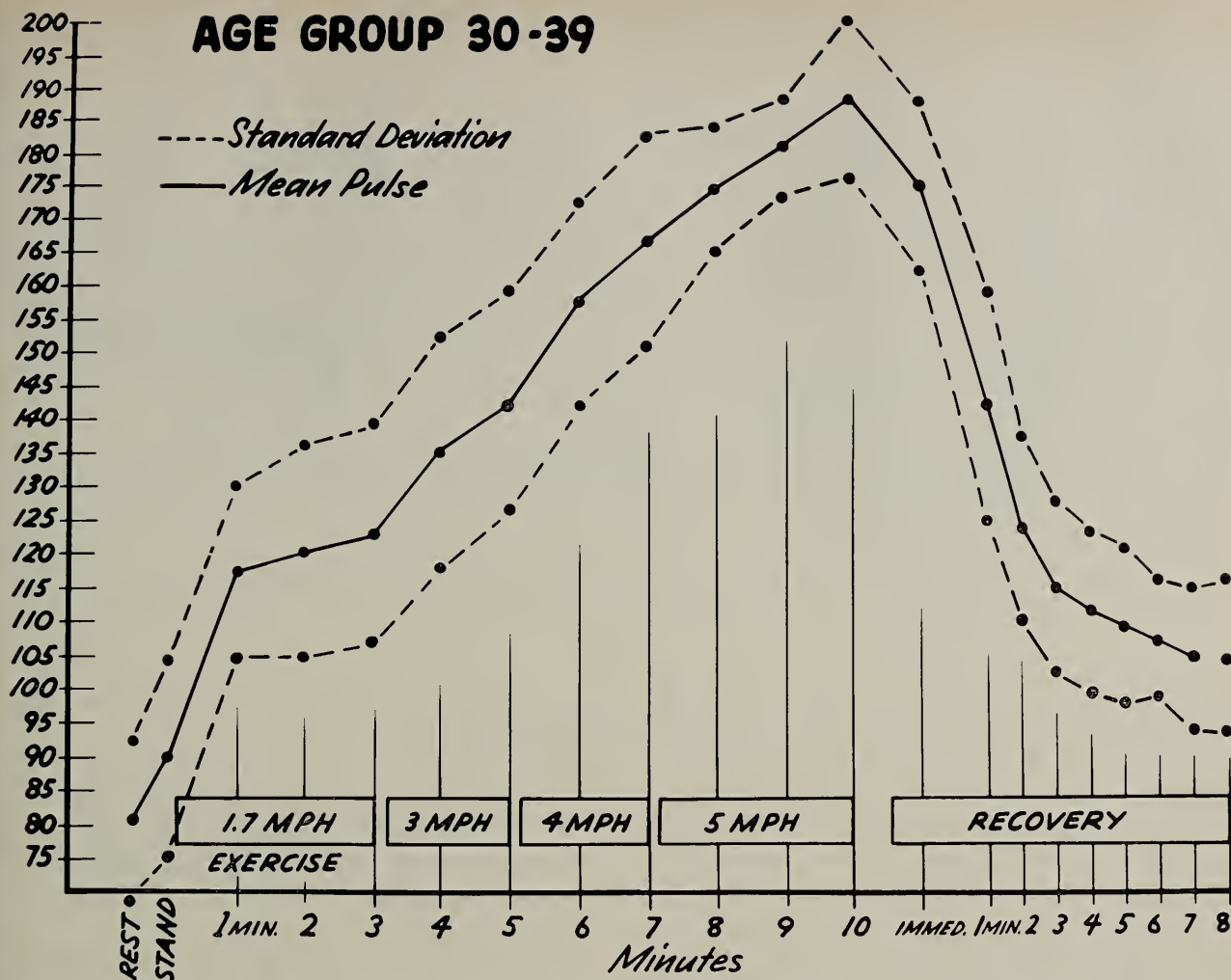


Chart 1. A group of 50 normal subjects in the age group 30 to 39 performed graded treadmill exercise and their pulse response during and after exercise was recorded at one-minute intervals. (Pulse rates are shown at the left edge of the chart.) While steady-state values are more evident at slower rates of exercise, maximal predicted pulse rates with fairly uniform standard deviations can be obtained.

grade. At this point, further exercise will put him into oxygen debt which will soon force him to terminate the test. One can be sure, however, that at this pulse rate he has reached his peak capability and that coronary insufficiency, if not seen at this pulse rate, will probably not be manifested in any circumstances of increased exercise, for cardiac work will not increase further. A good athlete, however, may not reach this pulse rate until he has covered a mile or more. In each case we are testing the maximum cardiac output but at far different levels of work accomplished.

If somewhere during the progressive increase in work activity, the demand for coronary flow is exceeded by the heart, characteristic changes in the electrocardiogram will develop and usually pain in the chest will follow. In about 40 per cent of patients we have observed with myocardial ischemia, pain does not develop. When the heart be-

comes ischemic, the cardiac output no longer increases; in fact it starts to fall. The left ventricular end-diastolic pressure rises and heart failure will rapidly ensue if further demands are made on the undernourished cardiac muscle. It is obvious that a previously prescribed level of exercise may fail to stress one patient enough and will overstress the next, so that when using treadmill stress testing as a case finder each patient should be pushed as far as necessary, but no farther than is safe.

Method

The patient to be evaluated is seated and a bipolar electrode is affixed to the upper part of the manubrium sternum and at the standard left chest V5 position. (Semler and coworkers⁹ found that postural T wave changes from supine to upright were less prevalent in a bipolar lead with reference electrode under the right clavicle. However, this

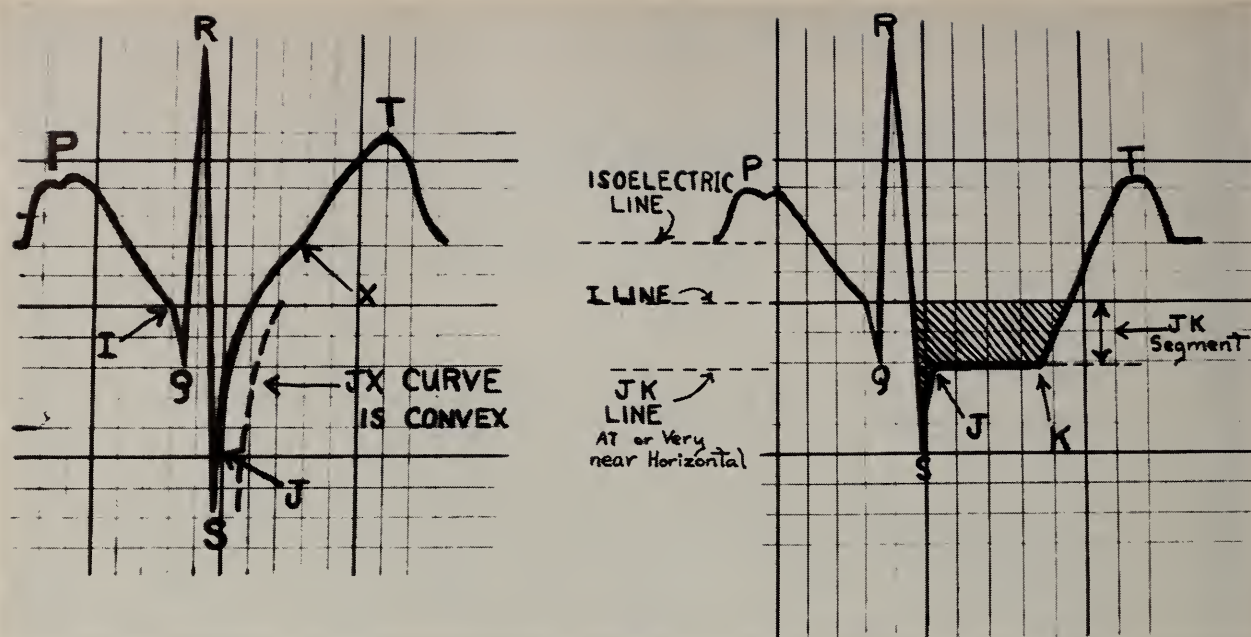


Figure 1.—The electrocardiogram complex on the left represents a normal response to exercise. J-point depression is a normal finding with convexity of the JX curve. The ECG complex on the right depicts an abnormal response to exercise and displays ischemic ST changes characterized by ST depression at least 2 mm below the isoelectric line, straightening of the J-K line and persistence of the ST depression for at least 0.08 second.

produces a slightly more anteriorly directed lead vector and would be less satisfactory for ST vector display.) A blood pressure cuff is affixed to the arm and an electrocardiogram is recorded in the sitting and standing positions together with blood pressure recordings. The patient is then allowed to step onto the treadmill, the speed of which is set at 1.7 MPH. The treadmill incline is a 10 per cent slope. With continuous oscilloscope monitoring of the patient's electrocardiogram, he is allowed to walk for 3 minutes at 1.7 MPH, then for 2 minutes at 3 MPH, 2 minutes at 4 MPH and finally 3 minutes at 5 MPH. If he is exhausted or if there should occur a fall in blood pressure or multiple premature ventricular contractions, the study is terminated. While the patient is walking on the treadmill, the blood pressure and the electrocardiogram strip is recorded at 1-minute intervals; and following exercise, electrocardiogram recordings and blood pressure measurements are made every minute for 8 minutes.

Interpretation

Abnormal ST depression is defined as a 2 mm depression, below the isoelectric line, that persists for at least 0.08 second (Figure 1). J-point depression is a normal finding after maximum exercise stress, and in fact has been alluded to by Robb and Marks¹⁷ as a finding associated with a lower mortality rate than the standard risk. A slow return of the

ST segment to the isoelectric line has been observed to be an early finding of ischemia and is interpreted as an equivocal finding. Further observation of this occurrence in larger numbers of patients will undoubtedly clarify this situation.

Two conditions which may cloud the interpretation of an exercise stress test are digitalization of the patient and complete left bundle branch block. In either case a false-positive treadmill stress test may result, and therefore patients who are receiving digitalis are requested to discontinue this medication one week before study of them is carried out.

To evaluate the patient's heart rate response to maximal exercise, a reference table is used which is a compilation of studies by Astrand, Robinson, Strandell, Norris and Ryhming²⁰ (Chart 2 and Table 1.) In this manner, the patient's percentage of predicted maximal heart rate can be obtained.

Application

The treadmill stress test can be employed in any situation in which objective evidence of ischemic heart disease is desired. We have done positive treadmill stress tests on completely asymptomatic persons and have recorded abnormal ST depressions occurring without chest pain in a significant number of them. In a recent study of 41 patients who had undergone a Vineberg-type operation for coronary revascularization it was of interest that only 35 per cent had abnormal electrocardiograms

HEART RATE IN MALES FOLLOWING EXERCISE

AGE (years)

| | 10 | 20 | 30 | 40 | 50 | 60 | 70 | 80 | 90 |
|------------------------------|-----|-----|------|-----|--------------|-----|-----|-----|----|
| ASTRAND | 210 | 197 | | | Maximal Work | | | | |
| | | | | | | | | | |
| Robinson | | 200 | 195 | 186 | 179 | 175 | 168 | 160 | |
| STRANDELL | | | | | | | | | |
| | | | | | | | | | |
| | | | 175 | 172 | 163 | 154 | 153 | 134 | |
| Norris, Shock, Yiengst | | | | | | | | | |
| | | | | | | | | | |
| | | | | | | 89 | | 95 | |
| Rything (Astrand) | | | | | | | | | |
| | | | | | | | | | |
| | | | | 115 | | 143 | | | |
| | | | ---- | | | | | | |

Chart 2. Heart rate responses to maximal and submaximal exercise have been reported at various age levels. It can be seen that while the older age groups have a reduction in maximal pulse rates, they have an increase in submaximal pulse rates. This physiological response to exercise is important in evaluating exercise stress studies since it is essential to know whether maximal or submaximal stress was employed.

TABLE 1.—Maximal Pulse Rates (M.P.R.) During Maximal Exercise for Patients of Various Ages

| Age | M.P.R. | Age | M.P.R. | Age | M.P.R. |
|---------|--------|---------|--------|---------|--------|
| 20..... | 200 | 41..... | 181 | 61..... | 167 |
| 21..... | 199 | 42..... | 180 | 62..... | 167 |
| 22..... | 198 | 43..... | 180 | 63..... | 166 |
| 23..... | 197 | 44..... | 180 | 64..... | 165 |
| 24..... | 196 | 45..... | 179 | 65..... | 164 |
| 25..... | 195 | 46..... | 178 | 66..... | 163 |
| 26..... | 194 | 47..... | 177 | 67..... | 162 |
| 27..... | 193 | 48..... | 177 | 68..... | 161 |
| 28..... | 192 | 49..... | 176 | 69..... | 161 |
| 29..... | 191 | 50..... | 175 | 70..... | 160 |
| 30..... | 190 | 51..... | 174 | 71..... | 160 |
| 31..... | 190 | 52..... | 173 | 72..... | 160 |
| 32..... | 189 | 53..... | 172 | 73..... | 160 |
| 33..... | 188 | 54..... | 171 | 74..... | 160 |
| 34..... | 187 | 55..... | 171 | 75..... | 160 |
| 35..... | 186 | 56..... | 170 | | |
| 36..... | 186 | 57..... | 170 | | |
| 37..... | 185 | 58..... | 169 | | |
| 38..... | 184 | 59..... | 168 | | |
| 39..... | 183 | 60..... | 168 | | |
| 40..... | 182 | | | | |

The above figures are based upon regression figures of Robinson (1938). Age groups from 10 yrs. to 20 yrs. have been compiled by Astrand and range from 210 M.P.R. to 197 M.P.R. respectively.

at rest. There were equal numbers of patients having normal electrocardiograms at rest and abnormal treadmill stress electrocardiograms before the Vineberg-type operation. This serves to emphasize the need for exercise stress testing in the evaluation of coronary artery disease.

The use of a regular exercise program in an attempt to improve myocardial tone and metabolism is currently being evaluated in many places,^{7,13,14} including Memorial Hospital of Long Beach. The treadmill exercise stress test, being an easily reproducible study, lends itself well to serial testing and evaluation of the myocardial response to exercise and changes which may occur during the course of the exercise program. It would also serve as a gauge of myocardial improvement in any program designed to improve coronary perfusion and myocardial metabolism.¹²

Ancillary Studies

The use of positional electrocardiogram responses has recently been studied in our laboratory and it is of interest that when an incompetent myocardium is overloaded by changing from the standing to the supine position, ST depressions are commonly encountered in patients with coronary artery disease (Figure 1). This is the result of increasing the venous return to the heart and will frequently bring out abnormal ST changes at a time when the sitting electrocardiogram is within normal limits. For this reason it is felt this maneuver should be included in the treadmill stress study.

It has been demonstrated by Sarnoff and co-workers¹⁸ that the tension time index is a very reli-

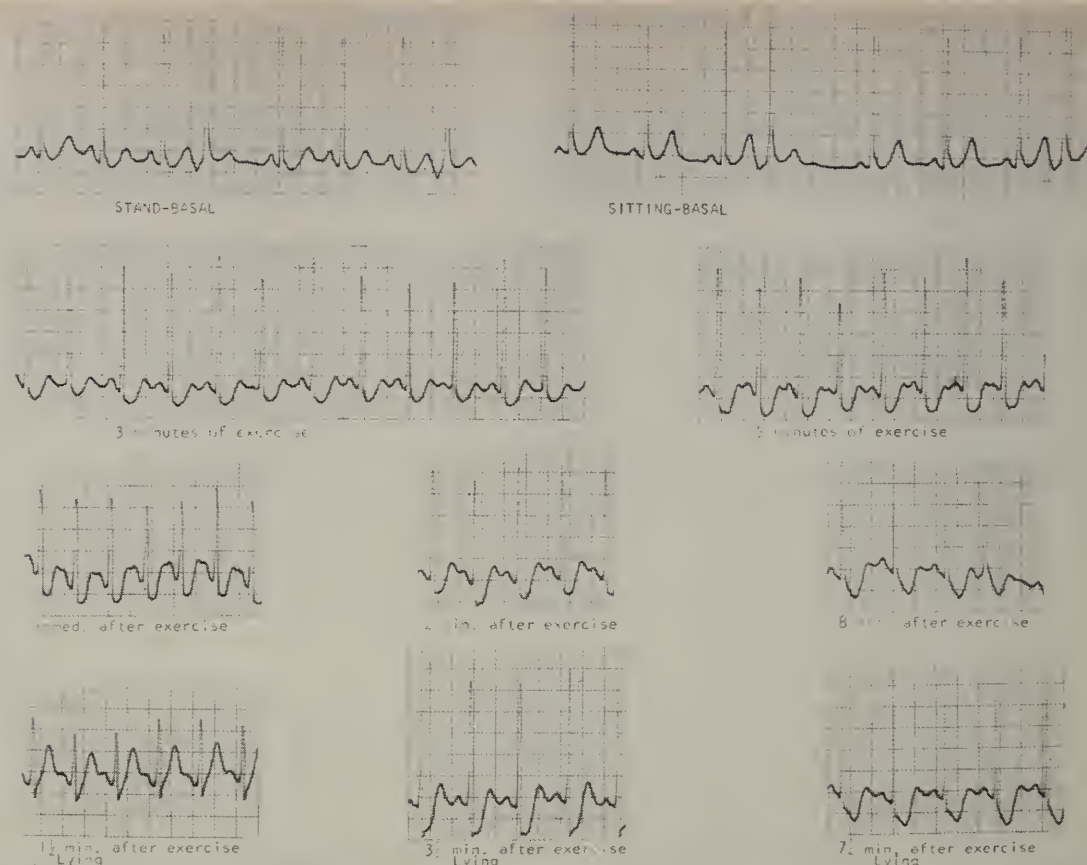


Figure 2.—Electrocardiogram of patient who had a quadrigeminal rhythm at rest. Immediately after exercise the ECG reveals a change from slow ST segment return to the baseline to normal J-point depression upon changing from sitting position to reclining. Two minutes after exercise ST depression is quite pronounced when reclining and eight minutes after exercise the sitting ECG reveals only a "strain configuration" of the ST segments while the reclining tracing demonstrates ST depression. This effect is not due to proximity changes of the heart to the chest wall, since similar findings were noted in both left lateral positions and supine positions.

able index of myocardial oxygen consumption. When the systolic blood pressure is multiplied by the pulse rate (which we call the modified time-tension index or M.T.T.I.) a close approximation of myocardial oxygen consumption is obtained. When using the treadmill for serial evaluations of a patient under treatment for ischemic heart disease, the changes in this measurement may be of more significance than the time of appearance of ST segment changes or chest pain. This is because differences in peripheral resistance and endogenous catecholamines may cause the heart to work harder to perform the same function (equivalent cardiac output) at one time than at another. Because of this, we look at the product of the systolic blood pressure and pulse rate as a function of cardiac efficiency when related to a certain work load and the pulse response as a function of physical conditioning as related to peripheral muscle metabolism.^{6,8} This is of course an oversimplification but the principle is useful nevertheless.

Chart 4 illustrates the changes in pulse and modified time tension index (product of systolic blood pressure and pulse) of a physician before and after a few weeks of physical conditioning. It can be seen that the pulse response is somewhat improved after physical conditioning (probably a very complex process) but also the heart is using less oxygen to accomplish more work as indicated by the product of systolic blood pressure and pulse (M.T.T.I.).

The graphs show the pulse curves and modified time-tension indices derived by the product of systolic blood pressure and pulse rate. These were recorded while the subject was exercising on a treadmill elevated to a 10 per cent grade. Chart 3 represents the pulse rate response before and after the training period and illustrates the profitable improvement in muscle efficiency in that less cardiac acceleration is required for a given work load. Chart 4 illustrates the improvement in M.T.T.I., after the training period, which reflects myocardial

oxygen consumption or cardiac efficiency.

Patients who have anginal episodes and positive treadmill stress tests, as evidenced by the production of abnormal ST depressions during or after exercise, may on occasion manifest greater tolerance to exercise and delayed ST changes following the administration of nitroglycerine sublingually. It may be that such patients, after administration of nitroglycerin could be allowed to exercise to a stage below that at which ST abnormalities occur. This can be correlated with the patient's pulse rate for a given amount of exercise and thereby allow the patient to pursue a physical rehabilitation program. Perhaps the response to nitroglycerine may also serve as an indicator for anticipated response to coronary revascularization procedures.

We have become interested in studying the isometric contraction time before and after exercise and this type of study is well adapted to treadmill stress testing. With a Sanborn four-channel writer, carotid pulse curves are obtained with simultaneous electrocardiogram and phonocardiogram. These tracings are recorded before and after maximal treadmill stress testing. The isometric contraction time is obtained by subtracting the ejection time (onset of upstroke of carotid pulse to the dirotic notch from the S1 to S2 interval of the phonocardiogram. Studies by Raab¹⁵ demonstrated that the cardiac sympathetic tone increases with decreasing physical activity, as demonstrated by a rising heart rate and shortening of the isometric period of the left ventricle at rest. He is currently utilizing heart rate and isometric tension periods during sensory and mental stress (noise, flicker light, mental arithmetic) as criteria for the prediction of myocardial ischemia-proneness and also the objective evaluation of reconditioning effects on the heart.¹⁶ This aspect of study should provide useful and easily obtainable information concerning myocardial function.

The use of apexcardiography before and after treadmill exercise stress testing may be a useful adjunct in the diagnosis of ischemic heart disease. It has been demonstrated by Benchimol and Diamond^{2,3} that prominent "a" waves in the apex cardiogram may occur in association with angina. This phenomenon is thought to be due to increased end-diastolic pressure in the left ventricle. As has been mentioned previously, many patients do not have associated pain subsequent to reduced myocardial function and any measures which will aid in detecting those patients having a compromised

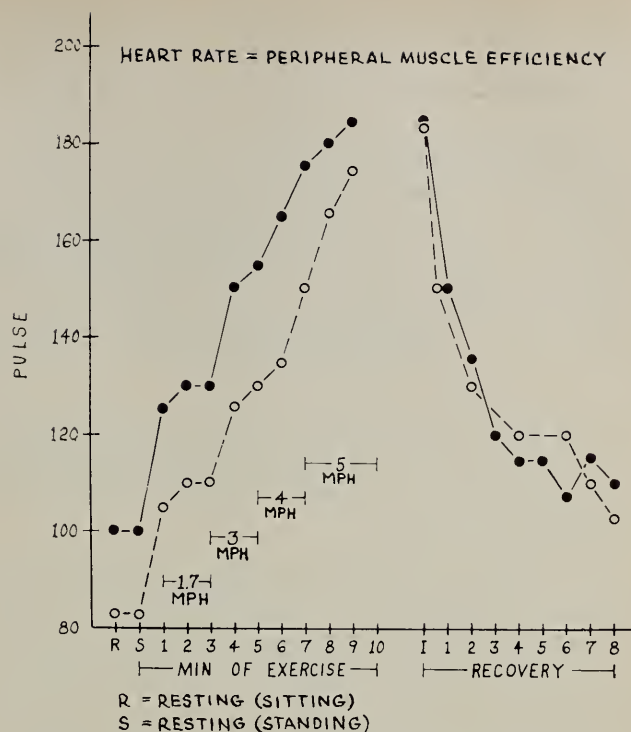


Chart 3. The straight lines on the graph represent responses before the subject underwent a period of physical conditioning (•) and the dotted lines represent responses after a period of conditioning (°). This graph displays the pulse rate response to graded treadmill exercise before and after a training period.

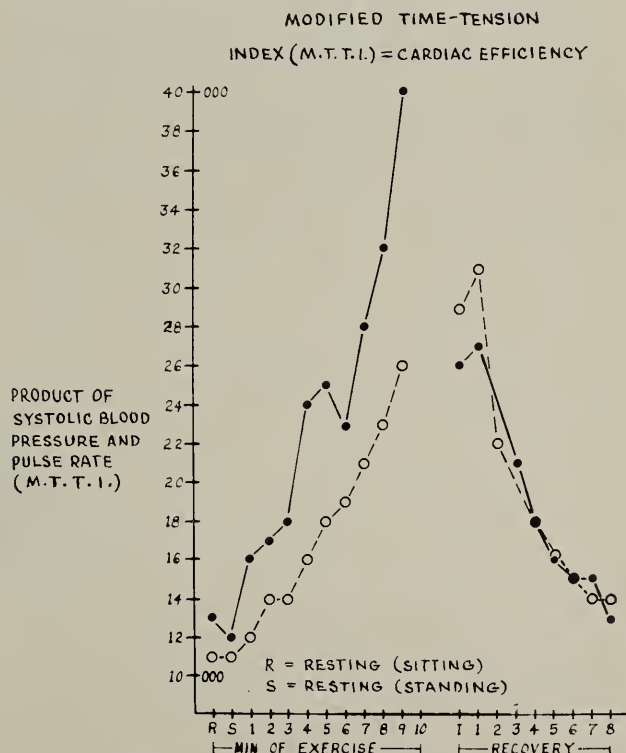


Chart 4. Same subject as in Chart 3. After nine minutes of treadmill exercise it can be seen that the graphic display after a period of physical conditioning reveals a reduced M.T.T.I. when compared with the graph before training (Chart 3). This suggests that after the training period the heart took 35 per cent less oxygen to do the same amount of work.

myocardium related to stress will be of considerable value in the overall assessment of their myocardial function. We have found a discovery rate of 11 per cent positive maximal treadmill stress tests in a clinically unsuspected group of 284 executives referred for routine examinations, and in an unselected group of 1,000 patients, the majority of males in all age groups having ischemic treadmill stress tests did so without associated pain. (To be published.)

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Linacre and Locke: Pillars of Medical Humanism

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■ *The following address was given by Dr. Cecil J. Watson at the Wm. J. Kerr Gold Headed Cane Lecture, University of California School of Medicine, on 9 June 1967. At this event on the eve of Commencement Day, the senior student who has been chosen by his classmates and by his professors in the Department of Medicine as the one who best exemplifies the qualities of a true physician is awarded a gold-headed cane.* This carries on the British tradition of a similar cane that was passed from physician to physician from 1689 to 1825. The original cane, which was carried successively by Doctors John Radcliffe, Richard Mead, Anthony Askew, David Pitcairn and Matthew Baillie, now rests in the Hall of the Royal College of Physicians in London.*

THE LIST of 20th century physicians who have previously participated in this Gold Headed Cane Lectureship at the University of California School of Medicine, San Francisco, is in many ways as illustrious as that of the six men who carried the cane in the 18th century. Distance in time also lends enchantment and perhaps this will be much more tangible in another two centuries. In any event you can understand the feeling of honor and privilege which I have in now joining the fine company of Gold Headed Cane Lecturers. For a number of years, as you know, this lectureship has honored Wm. J. Kerr, a distinguished physician and professor of medicine of happy memory in this school, a man whose friendship I long enjoyed,

and whose labor of love it was to found and for many years foster the tradition which is continued this evening.

The physicians who carried the Gold Headed Cane were by and large 18th century men. It is true that Radcliffe, whose cane it was in the first place, commenced his practice in the late 17th century, and Matthew Baillie, the last to carry it, finished his in the early 19th. Nevertheless, as the characteristics and achievements of individual centuries may be compared, theirs belong with the 18th. In general, the advancement of learning, to use the title of Francis Bacon's great work, was much more significant in the 16th, and especially the 17th, than in the 18th century. Little doubt that the science and culture of the gold headed canesmen were influenced in strong degree by the thinking of these giants of the earlier period who frequently exemplified the concept of the physician as a man of scholarly attainment as well as professional skills. I am particularly interested in the

*The award this year was made to two students, Robert I. Handin and Lorne G. Eltherington. Lawrence N. Hill was given honorable mention.

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Submitted 5 July 1967.

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natural philosophers of the 16th and 17th centuries and propose to tell you briefly something of the life and works of two of them whose thought has undoubtedly influenced physicians and scientists as well as philosophers of later times.

The Renaissance, it is generally agreed, had its focal point and much of its impetus in Florence, in the court of Lorenzo the Magnificent. It seems quite clear that Thomas Linacre of Canterbury was first and foremost in bringing the Renaissance to England. One can scarcely conceive of a finer example of how the forces of destiny at times serve a man and his country to their mutual advantage, nor of how a single man in 64 years can achieve in his own person such a remarkable synthesis of scholar and physician. With Thomas Browne and William Osler, of later ages, Linacre is at the summit of medical humanism. I have long cherished and often enjoyed a copy of Sir William Osler's Linacre Lecture of 1908, given at St. John's College, Cambridge. Nearly four centuries had then passed since the endowment by Linacre of lectureships in physic at Oxford and Cambridge. Linacre studied at Oxford but had no known attachment to Cambridge. Osler regards his bequest "as simply the act of a wise old man to encourage the study and teaching of medicine." The deed is a curious document, leaving a property known as the "Belle and Lanthorne" and 209 pounds in gold from which the College thenceforth was to pay 12 pounds a year for "a certayne lecture of physicke to be founded and established in the Universite of Cambridge." Every fourth year the lecturer was to cease his "Redying" for the space of half a year and he was to get only 6 pounds. Nothing is said as to the subject of the lecture but in the Statutes of Elizabeth, 1580, more precise directions are given. The lecturer was to be at the least, a Master of Arts, well versed in the works of Aristotle and somewhat also in those books of Galen which Linacre had translated into Latin. The office was continued in the Statutes of Queen Victoria, 1849, with even more explicit directions — "the lecturer to deliver *courses* on Foods and Drugs, on the Care of Health, on Methods of Healing, on Forensic Medicine." All this for 12 pounds a year.

The Court of Lorenzo de Medici

I hope you will agree with Samuel Johnson that biography is the cream of literature. In the sense that the biography of great men and contemporary history are inseparable, I accept Johnson's view

with pleasure. When Linacre was born, in 1460, the sanguinary Wars of the Roses in England were well under way, yet there is no evidence that their turbulence and bloodshed affected his early life and education. Selective service had not yet been devised but in any event, the semi-monastic life of the Universities appears to have offered sanctuary. In 1488, early in the reign of Henry VII, the wars over and England now relatively stable, young Linacre had completed his cloistered education at Oxford and the great world was about to unfold. He accompanied his old teacher, William deSelling, on an Embassy to Rome from Henry VII to the Pope. It is believed, however, that Linacre stopped in Bologna where he became the student of Poliziano, one of the great poets and scholars of the Renaissance, with whom he soon went to Florence to continue under his tutelage at the court of Lorenzo de Medici. Poliziano was one of Lorenzo's dearest friends; thus the young Englishman enjoyed the superb generosity for which Lorenzo was famous, and it may be noted that this reputation appears to have depended more on intellectual stimulus than physical comfort. Linacre was accorded the same privilege of instruction by Poliziano that was given to the sons of Lorenzo.

We may assume that it was not only the teaching of Poliziano that must have given joy and satisfaction to Linacre during this Florentine period. It is safe to say that Lorenzo was called the Magnificent because of his burning desire to learn and promote learning, his magnanimous spirit of inquiry, his love and fostering of art, literature and philosophy. Perhaps never since the golden age of Pericles, nor again until the "spacious days" of Queen Elizabeth I, was such a gathering of "master spirits" thus compressed in time and area. One contemplates the young Englishman's experience with a wistful feeling that a transmigration of souls might at times have its advantages. What a unique privilege it was for Linacre to sit at Lorenzo's board with even younger Michelangelo, drinking in the sparkling talk of the philosophers, Ficino and Pico della Mirandola; to know or even to see the great Florentine artists of the Renaissance, such as Botticelli, Perugino or Michelangelo's teacher, Ghirlandaio, and to see the marvels wrought by their predecessors, such as Ghiberti's golden doors of Paradise, or the cathedral dome of Brunelleschi. Linacre may have had occasional contact with that supreme genius, Leonardo da Vinci, although when Linacre was in Florence, Leonardo had already

transferred his activities to the court of the Duke of Milan. If any of you should wish to enjoy some delightful and highly informative reading about this time of great accomplishment, I recommend warmly the biography of the Medici, by G. F. Young.

The Influence of Scholars

Despite such surroundings and influences, or perhaps because of them, Linacre's profound humanism must have guided him more and more toward medicine during this period. He left Florence to spend a year in Rome, where he came under the influence of Hermolaus Barbarus, one of the outstanding scholars of his time. Osler believes that although Barbarus was not a physician, his intense interest in the works of Dioscorides, the first century pharmacologist, may have brushed off on Linacre and stimulated him to study medicine. At the same time, one may suspect that he was impelled by an urge to have a direct hand in a more practical humanism, the alleviation of suffering. Perhaps there was even a certain revulsion toward his Florentine period, and the intensive study of Greek in Lorenzo's Platonic Academy. He may well have felt that the Renaissance had too little immediate concern with the human problems which confront physicians. It is not certain when Linacre went to Padua to study medicine, but it is reasonably clear that he first spent a period of time in Venice working with Aldus, the great scholar and printer who credits Linacre with assistance in preparation of his superb edition of Aristotle. These volumes were issued in 1495-97. Thus Osler suggests that Linacre was in Venice at this time.

A friend and former student of mine, Dr. Ciro Dalla Rosa, at present a member of the medical faculty of Padua, has kindly ascertained from the records of the University that Linacre was examined and awarded the M.D. degree in 1496. He points out, however, that at that time it was unnecessary for a student to spend a long period in residence in order to qualify, and that many students came to Padua to be examined and receive its degree, after having had most of their education elsewhere. It is even possible that Linacre was then living in Venice and only went to Padua briefly to be examined and to receive the doctor's degree. This would mean that he must have picked up his medical education in Florence, Rome and Venice. In those days of strictly didactic lectures, this would not have been too difficult.

There is evidence that Linacre had returned to England well before 1500, as in that year he was made tutor to Prince Arthur, son of Henry VII, and it is clear that he had already spent some time at Oxford teaching grammar and practicing medicine. During this early period after his return from Italy, Linacre became teacher and lifelong friend of two men who were destined to be perhaps the greatest humanists of the 16th century, Desiderius Erasmus of Rotterdam and his friend, Sir Thomas More, whose *Utopia* brought him enduring fame. More, as you will remember, was the great chancellor who resisted Henry VIII and yielded his life for his principles. Erasmus' fame depends in part on his *Praise of Folly*, and if you have never read this delightful satire, it is something you will enjoy. Without naming Linacre, Erasmus is undoubtedly referring to him in this little book when he speaks of "an old Sophister that was a Grecian, a Latinist, a mathematician, a philosopher, a physician, and all to the greatest perfection." Linacre was also a priest, though not ordained until age 60.

The Royal College of Physicians

Earlier in his career, as physician to Henry VIII, his crowning glory was the founding of the Royal College of Physicians of London. Partly because of his great influence with the King, and with the help of Cardinal Wolsey, he obtained letters patent from Henry, dated 1518, constituting a corporate body of "regular-bred" physicians. This is the designation given later by MacMichael in his *Lives of British Physicians*, an excellent book upon which his later writing of the Gold Headed Cane was based. The sole authority of admitting persons to practice within the city of London and a circuit of seven miles around it, was granted to this corporation. The basis of the charter was stated as follows: "Before this period a great multitude of ignorant persons, of whom the greater part had no insight into physic nor in any other kind of learning; some could not even read the letter on the book, so far forth that common artificers, as smiths, weavers, and women, boldly and accustomedly took upon them great cures, to the high displeasure of God, great infamy of the faculty, and the grievous hurt, damage and destruction of many of the king's liege people." With these words, possibly Linacre's, the Royal College of Physicians was inaugurated, that institution with which the tradition of the Gold Headed Cane is so thoroughly entwined.

In the University of Padua, on a large wall of the famed and very beautiful Palazzo del Bo, are many full length, colorful portraits of great men who gained the M.D. degree in that school. Thomas Linacre makes a very impressive figure in a superb gown of what appears to be ermine and mink, and wearing a mitred hat. Next to him are Francis Walsingham, destined to be one of Queen Elizabeth's great ministers, and William Harvey who, as you know, was supreme among the early English medical scientists. Many other famous men of Renaissance medicine are also there. All of these and the marvelous portrait of Morgagni, which hangs in the elegant Salo of the Faculty of Medicine, cannot fail to impart a thrilling sense of the great history of Padua, especially in medicine, medical science and medical humanism. I hope that one day each of you will have the opportunity to share this sensation.

Seventeenth Century England

But I must now move into the 17th century, in many ways the greatest in the progress of English thought, and the advancement of learning, which occurred despite long continued civil turmoil, regicide, suppression of liberty and, finally, a revolution upon the success of which the stability of the next two centuries depended. The earlier years of the 17th were thrilling enough when one contemplates the enormous stimulus which Francis Bacon gave to science, Shakespeare and Milton to literature. In passing, one might include Shakespeare as a medical humanist, and on this point I refer you to a delightful book by a London surgeon, Mr. R. R. Simpson, entitled "Shakespeare in Medicine." But despite fearful troubles, the later years of the century can scarcely be said to have lagged behind, considering the enormous contributions of Isaac Newton, Thomas Sydenham, Robert Boyle, John Locke and many others who would grace any century. The organization of the Royal Society of London, chartered by Charles II, was actually an expression of the remarkable interest in the advancement of learning which was rampant in the days of the Restoration.

To any of you who might be interested in reading about this stirring period, I strongly recommend the fine book of Bronowski and Mazlish, published in 1960, entitled "The Western Intellectual Tradition," which spans the development of thought from Leonardo to Hegel and relates in delightful fashion the early history of the Royal Society and

the remarkable group which created it. Here you will find emphasized that there was no restriction of membership to scientists alone, and for many years, philosophers and poets, men such as John Dryden, were elected, as well as natural philosophers who combined scientific activity with exploration of human understanding. The poets were specifically charged with the duty of improving and invigorating the language of the Society. The two cultures, scientific and humanistic, had not yet become so unfortunately distinct as now. A pre-eminent example of this, at least among the charter members of the Royal Society, was John Locke about whom I wish now to comment briefly, as he would generally be placed at or near the pinnacle of medical humanism in the 17th century, and is undoubtedly one of the greatest representatives of all time.

John Locke's Philosophy

John Locke's philosophy, not his medicine, is the basis of his enduring fame. In America we recognize a debt to his *Essay on Human Understanding*, from which Thomas Jefferson, Benjamin Franklin, and perhaps others who helped write our Constitution, gained so much strength of ideology and beauty of expression. It is generally agreed that such phrases as "We hold these truths to be self evident . . ." were freely borrowed from Locke's great essays. Very little of his medicine has survived or deserved to survive as a contribution to the science or art, yet there is ample evidence that for many years he was a diligent, conscientious, imaginative physician, careful and compassionate in his ministrations. Here I refer you to a relatively new and delightful book entitled "John Locke, Philosopher and Physician," by Kenneth Dewhurst, a medical fellow of Corpus Christi College, Oxford. This book has much of interest for the physician and medical historian. There is no comparable record of the thoughts and observations of a physician whose friends included Robert Boyle, Thomas Sydenham, Thomas Willis and Isaac Newton.

In many ways Locke occupied a central communicative and stimulative role in this remarkable group. There is ample evidence that he was a close friend and confidant of Newton, the physicist, of Boyle, the chemist, and of Sydenham, the physician, and that he often sought advice from the latter in relation to problems encountered in his practice. During the earlier part of his 15 years

at Oxford, Locke taught grammar and philosophy, along with his study of medicine, but later devoted himself wholly to medicine and especially to pharmacology. Throughout his career, whether at home or abroad he kept ample notes of his observations and those of others, writing now in Latin, again in English, or in his own very efficient shorthand. His notes include many curious empiric remedies and prescriptions, either of his own device or acquired during his extensive travels in France and the later period of his exile in Holland. Though a strong empiricist and iatrochemist, he clearly predicted the modern approach, the use of specific remedies for each disease. In 1678 he wrote: "All doctors up to the present century seem to me to have failed because in the cure of disease, they have given little thought, or none at all, to the specific nature or peculiar ferment or fault (whatever in fact that is) of each disease, and considered solely the bile or phlegm . . . which are no more concerned with their specific natures than the type and richness of the soil is to the species of plants which may grow in it. Yet I have no doubt that to cure each type of disease, either a fixed method or fixed remedies are needed." Here Locke clearly contrasts the humoral pathology and empiricism which then held sway with the modern rationale of therapeutics. It is difficult to believe when reading his detailed prescriptions that he did not write them with tongue in cheek fully realizing how far removed they were from anything specific in terms of modern chemotherapy. At that time about the only remedies of any proven specificity were laudanum or tincture of opium for pain, the Peruvian bark or quinine for fevers, which we would now recognize as malarial and mercury for the pox, or syphilis.

An example of Locke's iatrochemistry, a prescription for gangrene: "Take strong vinegar 10 pints, good spirits of wine 4 pints, Slake in lime 2½ pints with *arsenic* 2 oz. in powder. *Stomach* also, in powder, 3 drachms. Stir all together for the space of three hours then let it settle for 4 or 5 hours, then pour off the clear supernatant fluid and add to it corrosive sublimate 1½ oz. and spirits of wine 1 pint, which being done store well and then bottle and shake it often during 3 or 4 years. It becomes of a deep amber color, and the older the better, for gangrene." According to this, to leave this poisonous concoction in the bottle permanently would be best and perhaps Locke recognized the double meaning of his directions.

Shortly after Locke left Oxford and went to London, he became associated in chemical experiments with Lord Ashley, also a member of the Royal Society. Quite soon Ashley had need of Locke as a physician. He suffered from recurrent abdominal pain, jaundice and a tender mass in the liver. This was "cauterized," after which there was copious drainage of "purulent matter containing many bags and skins." Two and a half centuries later Sir William Osler first pointed out that Locke's observations in this case actually constituted the first definitive description of hydatid or echinococcus cyst, a parasitic disease, which as you know is no longer endemic in England or the United States, but is still common in certain other parts of the world. It is remarkable that Locke achieved a cure in the case of Lord Ashley, thus preserving him for later service as Earl of Shaftesbury and Prime Minister of England. To effect this cure, Locke used a silver tube for long-term drainage and lavage. When Shaftesbury was later forced to flee England that he might escape the tyranny of James II, Locke was also obliged to go into exile in Holland. His medical and philosophical notes of this period are of great interest.

Locke and Medical Humanism

The first draft of Locke's great *Essay on Human Understanding* appeared in 1671. It is believed that this was stimulated by discussions, during the two preceding years, of a small group which met in Locke's rooms to talk about medical, philosophical and theological topics. More than half of the members were doctors, including Thomas Sydenham. Thus we may assume that the club and its discussions were truly representative of medical humanism. The final draft of the *Essay* was not to appear until 1690, after Locke's exile in Holland during which he devoted a great deal of time to the completion of this great work. After the revolution and the accession of William and Mary, Locke returned to England and for the remainder of his life devoted himself at various times to further writing on medical chemistry, philosophy and education. He died in 1704, probably as a result of right heart failure secondary to chronic bronchitis and emphysema. (Even in those days the problem of atmospheric pollution was recognized, and Locke, in fact, believed that the smog of London was a significant factor in the production of his asthmatic bronchitis.)

Locke was very modest about his contributions

to philosophy, speaking of himself "as an under-labourer in clearing the ground a little and removing some of the rubbish that lies in the way to knowledge." During the period that he lived in England, Voltaire, the great French philosopher, historian and satirist, knew Locke and admired him greatly. He spoke of Locke as a philosopher in the following words: "After so many speculative gentlemen had formed this romance of the soul, one truly wise man appeared who has in the most modest way imaginable, given us its real history. Mr. Locke has laid open to men the anatomy of his own soul just as some learned anatomist would have done that of the body."

I have given you this sketch of Linacre and Locke in the belief that their medical humanism must have had a great impact on the later Gold Headed Canesmen, just as it did on still later physicians and humanists, such as Oliver Wendell Holmes, Weir Mitchell, Sir William Osler and, much more recently, our dear departed friends, Bill Kerr and Jim Waring. As yet I have made no attempt to define medical humanism nor touch upon its significance for the practicing physician. Bronowski and Mazlish point out that the humanism of the Renaissance displayed a characteristic coupling of ideas and that this in particular gave it nobility: that classical literature is not an end in itself but expresses a wider love for man and nature. The physician who seeks for himself a broad humanistic culture over and beyond the science and art which he requires to minister to his patients is likely to become a medical humanist to the degree that he persists in seeking. Is it not evident that a doctor who is also a medical humanist will be more effective as a family friend and counselor, and will he not gain more lasting satisfaction in dealing with the problems of human relations which so often present? Humanism enlarges compassion and thus commands greater respect. We can only agree with Osler that the regular reading of great literature enriches the physician's life and broadens his understanding. The more scientific, less humanistic medicine becomes, the sooner it will be a trade rather than a noble profession. As Macauley said in speaking of the factors leading to the downfall of glorious Athens: "Each pursuit became first an art and then a trade. In proportion as the professors of each become more expert in their particular craft, they become less respectable in their general character. Their skill had been obtained at too great

expense to be employed only from disinterested views."

Medical Humanism Today

In recent times there has been a remarkable protest in the public press against what has been called the "sickly image" of the doctor in the mind's eye of the people. No matter how exaggerated this may seem to us, or how unwilling we might be to accept it, the medical profession and those responsible for medical education ought to examine the protest with care. I believe that with today's pressures to shorten the University medical curriculum and at the same time include the rapidly increasing body of technical information, the opportunity for the young man or woman entering medicine to gain a broad humanistic education is steadily being eroded. This applies to both pre-medical and medical curriculum. The latter includes essentially nothing in the way of continued formal offerings in the humanities. During the past five years an experiment has been in progress at Minnesota, consisting of monthly lectures given in the medical school, primarily for the medical students, by selected members of the Minnesota faculty in the humanities, or by visitors. Last year, for example, the mathematician-philosopher-historian, A. Bronowski, whose book I have already referred to, contributed a superb lecture, greatly enjoyed by the students. According to the plan of this program, a student should be able to hear 36 discussions by qualified lecturers, of various aspects of the humanities, during the four years of his medical curriculum.

But just as important, in my mind, is to halt the inroad on the humanities that is being made in the pre-medical curriculum. I have become increasingly convinced that a liberal, humanistic pre-medical education is essential if the physician is to mean as much to the people and to himself as we would all hope.

Osler, as many of you know, recommended a bedtime half-hour to strengthen the physician's cultural and humanistic attributes. It is safe to say that this habit regularly pursued will reduce the narrowness of an otherwise purely scientific culture. Osler's list of ten great books for the physician's bedtime half-hour includes "The Meditations of Marcus Aurelius," philosopher and Roman Emperor in the "Golden Age of the Empire" or the "Age of the Antonines" of which he was the second. No one can doubt that Marcus was a great

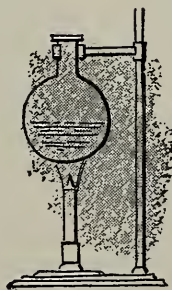
humanist, although this designation was still more than a millenium ahead. He had much to say about the soul, and his thoughts make clear that he would have equated humanism with a greater soul. For example: "Such as are thy habitual thoughts, such also will be the character of thy mind; for the soul is dyed by the thoughts. Dye it then with a continuous series of such thoughts as these: that where a man can live, there he can also live well. Things themselves touch not the soul, not in the least degree." And, from Epictetus, one of Marcus Aurelius' (as well as Osler's) favorite authors: "Be not a little soul bearing about a corpse."

Marcus Aurelius undoubtedly was asking what a man wanted to be like inwardly. He equated greatness of soul with the character of his father, Antoninus Pius. Those of you who have read Osler's magnificent essay, *Aequanimitas*, will remember that for him Antoninus epitomized the subject. Every physician ought to read and know Marcus Aurelius' fine description of the character of Antoninus. This could well serve in complementary fashion to the Hippocratic Oath or the Declaration of Geneva.

Let me close my talk with some of these lines. "Do everything as a disciple of Antoninus. Remember his constancy in every act which was conformable to reason, and his evenness in all things, the serenity of his countenance and his sweetness, his disregard of empty fame and his efforts to un-

derstand things, how he would never let anything pass without having first most carefully examined it and clearly understood it; and how he bore with those who blamed him unjustly without blaming them in return; how he did nothing in a hurry; and how he listened not to calumnies and how exact an examiner of manners and actions he was; and not given to reproach people, nor timid, nor suspicious . . .; and with how little he was satisfied, such as lodging, bed, dress, food, servants; . . . and how laborious and patient, and his firmness and uniformity in his friendships, and how he tolerated freedom of speech in those who opposed his opinions; and the pleasure that he had when any man showed him anything better. Imitate all this that thou mayest have as good a conscience when thy last hour comes, as he had." Little wonder that Antoninus had a sense of equanimity as he came to pass what he called the "flaming ramparts of the world."

And now let me add my warm congratulations to three who are to be signally honored here tonight in the Gold Headed Cane Ceremony to all of the members of this class of 1967 on your becoming doctors of medicine to your wives or husbands, your parents and teachers, all of whom have had such great interest in your progress these past four years. My best wishes to you and my hope that you will all be medical humanists as well as medical scientists.



CASE REPORTS

Nephrogenic Diabetes Insipidus Induced by Demethylchlortetracycline (Declomycin®)

DAVID E. TORIN, M.D., *Palo Alto*

TRANSIENT nephrogenic diabetes insipidus related to the ingestion of demethylchlortetracycline (Declomycin®, Ledermycin® in Europe) was first reported in 1965² and again in 1966.⁴ This is the third report of a patient in whom demethylchlortetracycline caused renal unresponsiveness to antidiuretic hormone.

Report of a Case

The patient, a 20-year-old college girl, came to the Stanford Cowell Student Health Center 7 February 1967 with complaint of thirst and of urinary frequency. Six weeks previously, consistent nocturia and nocturnal water drinking had begun. However, the patient felt perfectly well, was active in school and sports, and had only sought medical advice at the insistence of her boyfriend. Urinalysis of a specimen taken at the time of the first visit and of a first morning specimen taken the next day, were normal but specific gravity was 1.006 and 1.007, respectively. A more formal concentration test was then carried out, with no fluid being ingested for 16 hours. Specific gravity at 14, 15 and 16 hours was 1.009, 1.008 and 1.009. Ac-

cordingly, more intensive evaluation was begun.

The detailed history revealed no previous renal difficulty, but the patient had a problem with acne for several years. In March of 1965 she was treated with tetracycline, 500 mg daily for five days and then 250 mg daily for 40 days. As there was no improvement on this regimen, demethylchlortetracycline, 150 mg twice daily, was begun. At this point a severe sunburn developed after only modest exposure to sunlight and the drug was discontinued. The patient could recall no urinary difficulty during these six weeks.

In December 1966, demethylchlortetracycline was resumed, 150 mg twice daily. The supply was purchased anew and was not subjected to unusual heat. It was at about this time, although the exact time relationship is not remembered, that polydipsia and polyuria developed. Further history revealed that the patient was the youngest daughter of a 58-year-old mother. She and her mother did not get along well. In 1966 she had abdominal cramping pains temporally related to her going home for the summer vacation, with an exacerbation during Christmas vacation. Twice these symptoms subsided upon her return to the campus. Since urinary frequency had begun during her stay at home, a psychogenic factor was considered likely.

Mild fibrocystic disease of the breasts was first noted in January 1966, but had not been troublesome recently.

On physical examination the patient was noted to be thin, healthy and apparently emotionally normal. The pulse rate was 80, blood pressure 118/68 mm of mercury. In the entire examination, including visual fields, mild acne of the face and back was the only abnormality noted.

The diagnostic possibilities at this point included:³

1. Diabetes insipidus
 - (a) Lack of antidiuretic hormone
 - (b) Nephrogenic

Submitted 10 April 1967.

Reprint requests to: Palo Alto Medical Clinic, 300 Homer Avenue, Palo Alto 94301.

2. Psychogenic polydipsia
3. Diabetes mellitus
4. Chronic renal insufficiency
5. Hypercalcemic syndrome
6. Hypokalemic syndrome
7. Fanconi syndrome, acquired, secondary to degraded tetracycline products. (This syndrome has not been reported as being caused by demethylchlortetracycline, which is a more stable molecule than tetracycline.)⁵

Diagnostic tests and the results were as follows: Hemoglobin, 13.9 gm per 100 ml; packed cell volume, 42 per cent; leukocytes, 4,600 per cu mm — 34 per cent lymphocytes, 64 per cent neutrophils and 2 per cent monocytes. The erythrocyte sedimentation rate was 2 mm. Blood sugar 2 hours postprandial was 76 mg per 100 ml. Blood urea nitrogen was 13.5 mg and creatinine 0.95 mg per 100 ml. Serum chloride was 105 milliequivalents, sodium 144 milliequivalents, potassium 4.7 milliequivalents and carbon dioxide 24 milliequivalents per liter. Serum calcium was 10.3 mg per 100 ml. Creatinine clearance was 126 liters per 24 hours (1,730 ml per 24 hours urine volume). Urine alpha-amino nitrogen was 1.61 mg per kg per 24 hours (a normal value). A Venereal Disease Research Laboratory test was negative.

These normal results narrowed down the diagnostic choices to: (1) Diabetes insipidus due to lack of antidiuretic hormone (ADH) or acquired renal tubular inability to respond to ADH, or (2) psychogenic polydipsia.

To rule out lack of ADH and psychogenic polydipsia, the effect of intravenous vasopressin (Pitressin®) was tested. Usually, when diabetes insipidus is evaluated, the suspicion is that there is a lack of ADH. Thus, the Pitressin test is preceded by a determination of the changes in the urine concentration or osmolality during the intravenous infusion of 2.5 per cent or 3 per cent sodium chloride solution. However, if there is no renal response possible to Pitressin, the infusion of hypertonic saline is superfluous. Since renal unresponsiveness to ADH was a primary consideration in this patient, the Pitressin test was performed first. After a two-hour control period with water given ad lib, 20 milliunits (20/1000 of a unit) of Pitressin was injected intravenously. The rate of flow and the specific gravity of the urine were monitored during the two hours before and after the Pitressin injection. There was no change in either.

| Time | Urine Volume (Milliliters) | Volume Per Minute (Milliliters) | Specific Gravity |
|------------|----------------------------------------|------------------------------------|------------------|
| 9:03 a.m. | Void and Discard Urine | | |
| 9:34 | 85 | 2.7 | 1.007 |
| 10:05 | 88 | 2.8 | 1.009 |
| 10:35 | 81 | 2.7 | 1.010 |
| 11:05 | 99 | 3.3 | 1.009 |
| 11:10 | Pitressin, 20 milliunits intravenously | | |
| 11:26 | 72 | 3.4 | 1.010 |
| 11:41 | 40 | 2.7 | 1.010 |
| 11:57 | 47 | 3.0 | 1.006 |
| 12:14 p.m. | 47 | 2.8 | 1.007 |

The evidence so far gathered indicated that the problem was that of acquired renal tubular inability to respond to ADH. Therefore, demethylchlortetracycline was discontinued and the patient's course was observed. During the first week she slept undisturbed three times, although polydipsia continued. By 21 March, 25 days after the antibiotic was discontinued, she was asymptomatic. A concentration test was repeated: After 14 hours of fluid restriction, urine specific gravity was 1.016, and after 15 hours it was 1.020. At this point the test was discontinued.

Discussion

Two previous instances of demethylchlortetracycline apparently causing reversible nephrogenic diabetes insipidus have been reported.^{2,4} Demethylchlortetracycline has essentially the same antibacterial spectrum as tetracycline, but its increased half life means that lower doses are required.¹ The advantage of this different dosage is nebulous. To the well known disadvantage of photosensitization must now be added the hazard of nephrogenic diabetes insipidus.

Summary

Renal unresponsiveness to antidiuretic hormone developed in a 20-year-old girl while she was taking 300 mg daily of demethylchlortetracycline for control of acne. No other evidence of renal damage was found. Kidney function returned to normal within 25 days of discontinuing the medicine. A previous prolonged course of the same drug had produced no urinary symptoms, but had caused sun sensitivity.

GENERIC AND TRADE NAMES OF DRUGS

Demethylchlortetracycline—*Declomycin*.®
 Demethylchlortetracycline—*Ledermycin*.®
 Vasopressin—*Pitressin*.®

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The Rheumatic Manifestations of Rubella

A Report of Seven Cases

MORTON I. BROOKLER, M.D.
AND A. P. FUNK, M.D., *Downey*

SCATTERED CASE REPORTS have emphasized the occasional occurrence of arthritis as a complication of rubella.^{2,4,8} Few observers, however, have stressed the disproportion that may exist between the severity of subjective joint symptoms and the paucity of physical findings. The latter observation may reflect delay before the patient seeks medical aid as well as the brief duration of the disease.

The purpose of this report is two-fold, namely, to re-emphasize the fact that arthritis may not uncommonly complicate rubella, and to show that the severity of joint pain and tenderness may be in decided contrast to objective findings.

Reports of Cases

CASE 1.—A 14-year-old white boy was seen on 9 March 1964 with complaint of swollen glands and painful fingers of two days' duration. The preceding day, a diffuse pinkish rash had been noted on his chest and extremities, and at the same time he complained of soreness of the fingers, both feet and ankles, the soreness lasting only that day. The patient had had a sore throat one month previously, and this recurred with the onset of the rash.

Submitted 3 April 1967.

Reprint requests to: Gallatin Medical Group, 10720 South Paramount Boulevard, Downey 90241 (Dr. Brookler).

On physical examination a fine pinkish macular eruption was noted on the lower extremities and anterior chest. The patient also had a malar flush and the body temperature was 37.5°C (99.4°F). The throat showed slight erythema without exudate. The right wrist was slightly swollen as were the proximal interphalangeal joints of the index, long and ring fingers of the right hand. These joints were extremely tender, especially on the palmar aspect of the hand. The second to fourth toes were tender bilaterally without definite swelling. The ankles were slightly tender but not objectively swollen. Shotty, slightly tender inguinal and posterior auricular lymphadenopathy was present. The liver and spleen were not palpable. Examination of the heart and lungs revealed no abnormality.

Laboratory studies revealed hemoglobin of 14.6 gm per 100 ml. Leukocytes numbered 5,100 per cu mm with 70 per cent lymphocytes, a few atypical. The sedimentation rate was 4 mm in one hour (Westergren) and the antistreptolysin titer was 125 units. The result of a slide latex test was negative for rheumatoid factor. A culture of material from the throat grew alpha non-hemolytic streptococci.

Treatment consisted of Ascriptin® 10 grains five times a day, bed rest and penicillin G by mouth, 400,000 units four times a day, for ten days.

The patient returned nine days later, 18 March, feeling much better although the interphalangeal joints were still slightly tender and swollen. One week later he was completely asymptomatic.

CASE 2.—A 22-year-old white woman was seen 3 June 1964 with swelling and stiffness of both hands of one day's duration. Typical German measles had been diagnosed on 30 May.

Physical examination revealed mild swelling of the proximal interphalangeal joints of both hands. The palmar aspect of the joints and just proximal to the joints was very tender. No lymphadenopathy was noted.

Hemoglobin was 10.4 gm per 100 ml of blood. Leukocytes numbered 5,100 per cu mm with 48 per cent lymphocytes, a few atypical. The sedimentation rate was 26 mm in one hour (Westergren) and the latex slide test for rheumatoid factor was non-reactive.

Treated conservatively with Ascriptin® 10 grains every four hours and bed rest, the patient became

*Two parts aspirin, one part magnesium-aluminum hydroxide.

asymptomatic within seven days of the initial examination.

CASE 3.—A 19-year-old white girl was seen 13 May 1964 because of swollen and stiff hands. Four weeks earlier, German measles was diagnosed. Three days after the onset of the rash, swelling of the proximal interphalangeal joints of the left hand developed and lasted for one week. As the left hand cleared, swelling of the right wrist and hand developed.

On physical examination, mild swelling of the proximal interphalangeal joints of both hands, with a great deal of tenderness of the palmar aspect of these joints, was observed. No other abnormalities were noted.

Laboratory studies showed hemoglobin of 15 gm per 100 ml of blood and leukocytes numbering 9,200 with 34 per cent lymphocytes. The sedimentation rate was 8 mm in one hour (Westergren) and a latex slide test for rheumatoid arthritis and a clot test for lupus erythematosus were negative.

Ascriptin® was prescribed and the patient became completely asymptomatic in ten days.

CASE 4.—A 20-year-old white woman was first seen 13 June 1964 because of pain in the hands. Five days before, post-occipital lymphadenopathy and generalized macular rash had developed, the latter lasting two days. Pain in the hands began the day the rash disappeared.

Diffuse periorbital puffiness with bilateral tender occipital lymphadenopathy was noted on physical examination. There was also puffiness of the proximal interphalangeal joints of both hands and the third and fourth metacarpal joints of the right hand.

Hemoglobin was 14.5 gm per 100 ml of blood. There were 5,600 leukocytes per cu mm with 49 per cent lymphocytes, a few atypical. The sedimentation rate was 35 mm in one hour (Westergren) and the latex slide test was non-reactive.

The patient was treated with Ascriptin® and bed rest and three days later the joints were much improved as was the lymphadenopathy. On 22 June, nine days after she was initially seen, she was completely asymptomatic.

CASE 5.—A 47-year-old white woman was seen on 9 July 1964 because of a diffuse rash and swelling of the hands. The rash had occurred three days previously and approximately two and one-half weeks after she was exposed to a neighbor's child

with German measles. One day after the onset of the rash the patient had body temperature of 38.8° C (102°F) and complained of sore throat. The next day swelling and pain developed in both hands and there was a burning sensation in the palms.

Subsiding measles-like rash on the legs with swelling of the proximal interphalangeal joints of both hands, especially the ring and middle fingers, was noted on physical examination. There was extreme tenderness of the palmar aspect of all the proximal interphalangeal joints.

Hemoglobin was 13.3 gm per 100 ml of blood. Leukocytes numbered 6,000 with 30 per cent lymphocytes. The sedimentation rate was 25 mm in one hour and the latex slide test was non-reactive.

Swelling of both wrists and ankles developed the day after the patient was first seen but she became completely asymptomatic within the next seven days while taking Ascriptin® and resting in bed.

CASE 6.—An 18-year-old white boy student was first seen 17 March 1966 with complaint of sore throat and swelling of hands and face. Fever and a faint maculopapular rash had begun three days earlier and they subsided simultaneously.

Physical examination revealed bilateral cervical adenopathy and swelling of both wrists and the metacarpal and proximal interphalangeal joints bilaterally. A small effusion was present in the right knee. The throat showed no erythema or exudate.

Laboratory examination showed a hemoglobin of 15 gm per 100 ml of blood. Leukocytes numbered 5,400 per cu mm with 56 per cent lymphocytes, a few atypical. A culture of material from the throat grew no pathogens. The sedimentation rate was 10 mm in one hour (Westergren). A latex slide test for rheumatoid arthritis and a clot test for lupus erythematosus were negative.

Ascriptin® and bed rest were prescribed and the patient became asymptomatic in four days.

CASE 7.—A 22-year-old white woman was seen 10 February 1966 with a maculopapular diffuse rash typical of German measles. The day before the rash appeared she noted stiffness and swelling of the hands.

On physical examination swelling and mild tenderness of the second and third interphalangeal joints of both hands were noted. A small effusion in the left knee also was observed.

Hemoglobin content was 14 gm per 100 ml of blood and leukocytes numbered 4,700 with 47 per

cent lymphocytes. The sedimentation rate was 30 mm in one hour. A latex slide test for rheumatoid arthritis and a clot test for lupus erythematosus were negative.

Treated with Ascriptin® and bed rest, the patient was asymptomatic three days after she was first observed.

Comments

As exemplified by the seven cases herein and those previously reported, the rheumatic complications of rubella are limited to young adults and run a benign transient course. Symptoms referable to the joints follow or appear with the rash, the small joints of the hands being most frequently involved. Noteworthy was the severity of pain and tenderness in the palmar aspect of the proximal interphalangeal joints in the presence of minimal objective findings.

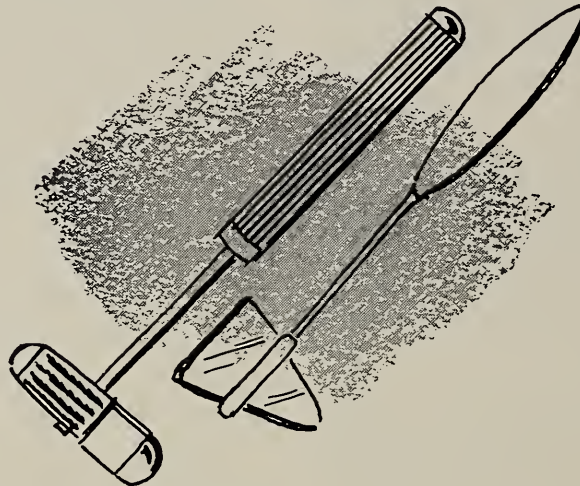
Treatment is entirely symptomatic—a conservative program of rest and salicylates.

Summary

The rheumatic manifestations of rubella as they occurred in seven observed cases have been reported.

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Herpes Simplex Meningoencephalitis

These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California Medical Center, San Francisco. Taken from transcriptions, they are prepared by Drs. Martin J. Cline and Hibbard E. Williams, Assistant Professors of Medicine, under the direction of Dr. Lloyd H. Smith, Jr., Professor of Medicine and Chairman of the Department of Medicine.

DR. DYKMAN*: The patient is a 55-year-old housewife with a history of alcoholism who was referred to the Neurology Service for evaluation. She was relatively well until 4 or 5 February 1966. At that time, drinking vodka, she experienced headache and anorexia and vomited. On 7 February at 7 a.m. she fell in the bathroom but did not lose consciousness and did not appear to have a head injury. She went back to bed and within a half hour had the first of three seizures. Subsequently she was confused but not hyperactive. She was admitted to hospital in her community with a diagnosis of delirium tremens. Her mental and neurologic status gradually deteriorated, as indicated by rejection of assistance and by muteness, apathy and incoordination in feeding herself. She became febrile, with a maximum temperature of 40°C (104°F). A lumbar puncture was performed on the tenth day of her illness. The spinal fluid contained 48 white blood cells per cu mm (73 per cent of them were lymphocytes), 70 mg of protein and 64 mg of glucose per 100 ml. A culture was negative. The patient was transferred to another hospital on day 16 and a cerebral arteriogram was performed. This was considered normal with a minor exception which will be discussed by the radiologist, and she was transferred to the University of California Hospital on day 18.

On admission she was awake but unable to speak and was more profoundly withdrawn than previously described. She was incapable of caring for herself. The temperature on the day of admission ranged from 38° to 39.7°C. Leftsided weakness, spasticity and decreased sensation of the face, including the cornea, were noted on physical examination. Neck stiffness was observed by one observer on the day of admission but not confirmed

or observed again. After admission, the patient had a seizure which began in the left hand, and had deviation of the head and the eyes to the left. Lumbar puncture was performed and the opening pressure was 175 mm of water. There were 133 lymphocytes per cu mm of fluid and 126 mg per cent of protein and 54 mg per cent of glucose per 100 ml. Culture of the spinal fluid, examination with India ink, and smears for acid-fast bacilli and fungi were negative. The spinal fluid contained a few crenated red cells and was slightly xanthochromic. The blood leukocyte count was 8,600 per cu mm with 72 per cent neutrophils. The sedimentation rate (Westergren) was 31 mm in one hour. Liver function tests were normal. An electroencephalogram showed diffuse slowing with a right focal spiking. Skin tests for tuberculosis and fungi were negative.

Serologic tests for viral antibodies were performed by the Virus and Rickettsial Disease Laboratory of the California State Department of Public Health. Complement fixing antibodies against herpes simplex rose from 1:32 (day 20) to 1:128 (day 32 of illness). This four-fold rise in complement fixation titer in two weeks was considered diagnostic. Complement fixation tests for antibodies against poliomyelitis virus Types I, II, III, influenza virus Types A and B and mumps virus were negative.

A second electroencephalogram showed diffuse slowing with left midtemporal spiking. The patient's mental status gradually improved and she was discharged on the 47th day to a convalescent hospital. At the time of discharge, she was able to answer a few simple questions and could feed herself but was still unable to remember recent events and was resistant to acts of aid. Her state could be considered one of mute and apathetic dementia,

*Lynn E. Dykman, M.D., Resident in Medicine.

less severe at discharge than upon admission. The left hemiparesis was improved but not completely absent.

DR. RUSSELL*¹: The x-ray films show only a few things worth commenting on. I do not believe that they are related to the patient's illness. Carotid arteriograms were done 16 days after the onset of illness. Injection by way of the right side was remarkable only in that the anterior cerebral artery did not fill; otherwise it was a perfectly normal pattern. Injection by way of the left side showed filling of both anterior cerebral arteries from the left, which was due to a minor congenital anomaly. The initial film of the chest was unremarkable, but a repeat film done three days later showed a small, faint density in the left costophrenic sulcus which was thought to be an area of discoid atelectasis.

DR. CROCKER*²: Thank you Dr. Russell and Dr. Dykman.

The Diagnosis

Several diagnostic possibilities were considered as the patient was under the care of physicians in Hanford and in two San Francisco hospitals. All of the alternatives were appropriate to the living pattern of the patient before the onset of her illness or to the disease itself. Pertinent diagnoses will be discussed in the order in which they arose:

1. *Alcoholic encephalopathy*

Alcoholic brain disorders were first considered in the course of this patient's illness. She was an habitual daily user of some quantity of vodka. Vomiting was followed by anorexia and she stopped drinking. Two days later she fell in the bathroom and then had three left-sided seizures. She was admitted to a Hanford hospital with a diagnosis of delirium tremens.

Delirium tremens occurs upon withdrawal from alcohol for two to five days and usually comes after some accelerated rate of drinking. Nausea and vomiting are followed by inability to drink for a few days, at which point the manifestations of withdrawal from alcohol occur. Tremulousness and visual hallucinosis are common. Disorientation and confusion occur and such patients are often physically quite active. A small group of alcoholics has been noted in which "alcoholic epilepsy" or "rum fits" follow a period of withdrawal. Seizures may occur alone or may be ac-

companied by manifestations of delirium tremens.¹⁸

Since the initial findings in the patient were that she had been a continuous drinker and that following a period of withdrawal, a fall and seizures had occurred, not associated with tremor, hallucinations or the active phenomena of delirium tremens but rather inactivity, withdrawal and confusion, the diagnosis of delirium tremens might be less appropriate than "alcoholic epilepsy" without evident typical delirium tremens.

Nutritional disorders of the central nervous system are commonly associated with alcoholism and may lead to the Wernicke syndrome, which is specifically related to thiamine deficiency. This encephalopathy is characterized by ocular palsies, nystagmus, ataxia (which is more evident in the "heel-to-shin" test than in the "finger-to-nose" test), impaired memory, withdrawal, muteness and irrationality.¹⁸

Some of these findings, particularly the last three, were present in this patient when she was admitted to Hanford Hospital and were present on her arrival here; some persisted as she left Moffitt Hospital. Thus, manifestations compatible with alcoholic central nervous system disorders were present in this patient but alcoholism alone would not account for the subsequent clinical findings, particularly those in the cerebrospinal fluid.

2. *Head injury or subdural hematoma*

The possibility of acute brain trauma or subdural hematoma was introduced by the patient's fall in the bathroom followed shortly by three left-sided seizures. She had no visible bruise or scalp swelling, but this would not exclude a significant cerebral injury.

Subdural hematoma develops some time after a head injury and gives rise to headache, focal neurologic signs, fluctuations in the state of consciousness and seizures. Subdural hematoma is not responsible for fever unless there is blood in the cerebrospinal fluid. In periods of consciousness, the patient's mental state may be fairly clear or decidedly confused. Subdural hematoma is not uncommon among alcoholics and the clinical course may be modified either by signs and symptoms arising from alcoholic brain disease or by the greater capacity of the cranium to accept an added volume of blood because the volume of the brain is reduced by atrophy. Thus, until fever began, this patient's state could have been due to hematoma superimposed on alcoholic encephalopathy.

Finally, the fall may have represented the first

*¹Warren M. Russell, M.D., Assistant Professor of Radiology.

*²T. Timothy Crocker, M.D., Professor of Medicine.

seizure in a series rather than the cause of the subsequent convulsions.

As the two initial diagnoses of alcoholic brain disease and recent or past head injury were being considered, fever developed. The spinal fluid findings already described led to transfer to a San Francisco hospital, where the clinical and cerebrospinal fluid findings were confirmed and an arteriogram was done. Thereupon the patient was moved to the Neurology Service of Moffitt Hospital. At this time, the foremost diagnostic alternatives were viral meningoencephalitis and brain abscess; purulent meningitis was not a very significant possibility, but was appropriately pursued.

3. Primary purulent meningitis

Neck stiffness was equivocally present on one examination only. This is a valuable negative sign, for it reduces the probability of primary meningitis, either viral or bacterial. Signs of meningeal irritation may be absent in herpes simplex virus meningoencephalitis and in brain abscess. Purulent meningitis was further reduced in likelihood by negative smear and culture studies of spinal fluid, by the low cell count and the normal glucose content of the fluid. Simple purulent meningitis was considered to be insufficient to cause the dementia or a right motor cortical lesion leading to left-sided seizures and hemiparesis. Generalized and focal dysrhythmias were noted in the electroencephalogram, compatible with diffuse and focal cerebral changes. These signs indicated that if the meninges were involved the involvement was part of a more extensive process.

4. Brain abscess

This diagnostic possibility was raised for several reasons, each of which is discussed below.

Localized cerebral involvement. A focal change in the right motor cortex was observed by electroencephalography, and left-sided focal convulsions, weakness and sensory loss were present. Skull films, a brain scan and cerebral arteriograms did not reveal a focal lesion. Brain abscess, although it produces localizing findings, stupor or coma, does not usually produce personality disorders with the degree of withdrawal and loss of psychological integration that was present in this case. The sum of these findings is an indication of widespread cerebral involvement with focal changes in the right hemisphere. Brain abscess superimposed on alcoholic encephalopathy could bring about all the abnormalities noted in this patient. However, the

generalized nature of the findings made it essential to consider viral meningoencephalitis, while efforts to localize an abscess were undertaken as required by the localizing findings.

Cerebrospinal fluid findings. Loesser and Scheinberg¹³ observed normal cell counts in 21 of 70 patients with brain abscess, and in the rest of the group counts ranged from very low to as high as one thousand. Such cell counts were regarded as less compatible with primary purulent meningitis and as more indicative of neighborhood reactions to an abscess near the meninges. The numbers of cells found in spinal fluid of patients with brain abscess overlap with the numbers found in herpes simplex virus meningoencephalitis.^{12,15}

Spinal fluid protein measurements were normal in a small proportion of Loesser's and Scheinberg's cases of brain abscess and were elevated only to a moderate degree among most of the remainder. The protein content of spinal fluid from cases of viral meningoencephalitis would overlap with the values for brain abscess.^{12,15} Finally, the sugar content of the cerebrospinal fluid was low in a very small proportion, normal in the majority of patients with brain abscess¹³ and normal in herpes simplex meningoencephalitis.^{12,15} The intracranial pressure was often increased in brain abscess, but this is also noted with viral meningoencephalitis.

In differentiating among brain abscess, purulent meningitis and viral central nervous system infection, the low cell count and normal sugar content of the spinal fluid are compatible with both brain abscess and viral infection but help in excluding bacterial and fungal meningitis, in which the glucose content of the spinal fluid is characteristically low while the cell count is commonly higher than in brain abscess or viral meningitis or encephalitis.

5. Other known or presumed viral infections of the central nervous system

Arboviruses. In the western United States, the viruses of Eastern Equine Encephalomyelitis, Western Equine Encephalomyelitis, St. Louis Encephalomyelitis and a more recently discovered arbovirus, the California Virus,⁹ cause meningoencephalitis, but only during the mosquito season, which extends from May through August. Our patient could not have been infected with one of these agents in February.

Rabies virus. Rabies occurs in all seasons but the clinical course is not that of meningoencephalitis. Rabies follows an animal bite, does not interfere with consciousness, progressively interferes

with motor function and terminates with absence of the ability to swallow but the sensorium clear. Convulsions may occur terminally, associated with impaired consciousness, but at this time impairments of motor function are diagnostic.

Lymphocytic choriomeningitis virus. Diffuse cerebritis and very high spinal fluid cell counts occur in man infected by this mouse virus. There have been no cases in California in over 20 years and routine serologic search for this virus was discontinued in 1964 by the State Department of Health Laboratory of Viral and Rickettsial Diseases, although serologic tests are available if specifically requested.

Enteroviruses. The enteroviruses are known to produce encephalomyelitis, but more commonly to produce meningitis with or without anterior horn cell changes. The predominant lesion of the brain is not in the cortex but is in motor ganglia of the bulb. Paralysis of respiratory and cranial nerve function are not accompanied by upper motor neuron signs.

Encephalomyelitides of presumed viral origin. (a) Encephalitis lethargica has not been reported since 1934 and had passed the peak of reported cases by about 1927.⁵ It remains a disease of unknown but possible viral origin and was considered to represent encephalomyelitis due to influenza virus infection at the time of the original report by Von Economo in 1917. Neurologic disorders have been associated with influenza virus infection in more recent times,^{7,10} and add weight to the concept of Von Economo.

Serologic tests for influenza virus infection were negative in our patient.

(b) Inclusion body encephalitis of Dawson, reported in 1934 and seen repeatedly since, is a subacute or chronic progressive involvement of the brain leading to autopsy findings of intranuclear inclusion bodies in cells of the cerebrum after formalin fixation and staining with hematoxylin and eosin.⁵ The inclusion bodies are indistinguishable from the nuclear inclusions of the *Herpesviruses* by light microscopy but have been found by electron microscopy¹⁷ to contain structures identical with the large pseudomyxoviruses (measles-distemper-rinderpest group). Correlation with measles antibody suggests etiologic association of this disease with viruses other than *Herpesviruses*.

Herpes simplex virus infection in this patient will

TABLE 1.—*Herpes Simplex Encephalitis: Report of 20 Cases—Incidence of Signs and Symptoms**

| Signs and Symptoms | Cases |
|---------------------------------|-------|
| Early Symptoms | No. |
| Headache | 6 |
| Lethargy-weakness | 6 |
| Myalgia | 5 |
| Speech difficulty | 5 |
| Anorexia, nausea, and vomiting | 4 |
| Sore throat | 3 |
| Irritability-restlessness | 2 |
| Signs | |
| Mental confusion-stupor | 13 |
| Coma | 10 |
| Twitchings-convulsions | 8 |
| Herpetic stomatitis | 6 |
| Increased intracranial pressure | 3 |
| Paralysis | 1 |

* From Miller, Hesser and Tompkins¹⁵

be discussed below.

(c) Demyelinating encephalitis may occur after viral enantheams and exantheams, after vaccination against smallpox or rabies, and possibly following influenza.⁷

No history of predisposing exposure or illness was elicited or discovered in this patient; hence this pathogenetic phenomenon will be set aside except as demyelination may occur in herpes simplex virus encephalomyelitis.

6. *Herpes Simplex Virus meningoencephalitis*

In 20 cases reported by Miller, Hesser and Tompkins¹⁵ early symptoms included headache, lethargy or irritability and restlessness, weakness, myalgia, speech difficulty, anorexia, nausea and vomiting and sore throat (Table 1). Fever, increased cerebrospinal fluid protein and mononuclear pleocytosis were present in all patients. Additional signs in varying frequency among the reported cases included confusion, stupor and coma, increased intracranial pressure, twitching, convulsions and paralysis.

Herpetic stomatitis was present in six cases only, but was accompanied by sore throat in three and was considered as being gingivostomatitis. This is usually part of a primary infection by herpes simplex virus. Lesions of recurrent labial herpes had not occurred in the past history and were not present in the acute phase of illness in the remaining patients. These observers concluded that herpes simplex virus encephalitis occurs as part of a primary infection, with or without the typical primary gingivostomatitis.

Increased intracranial pressure was not com-

TABLE 2.—*Methods of Diagnosis of the Cases of Herpes Simplex Encephalitis**

| Method | Patient | Age (years) | Sex | Erythrocytes in | Type A | Rise | Outcome | |
|--------------------------------------------------------------------|---------|----------------|-----|--------------------|-----------------|------------------|---------|-----------|
| | | | | Spinal Fluid | Inclu- sions | in Antibodies | Died | Recovered |
| Isolation of virus (Six cases) | 1 | 10 | M | | | X | X | |
| | 2 | 29 | F | X | X | | X | |
| | 3 | 27 | M | | | | X | |
| | 4 | 54 | M | | | | X | |
| | 5 | 37 | M | X | X | | X | |
| | 6 | 58 | M | X | X | X | X | |
| Inclusion in brain (Four cases) | 7 | 52 | F | X | X | | X | |
| | 8 | 60 | F | | X | | X | |
| | 9 | 48 | F | X | X | X | X | |
| | 10 | | M | X | X | X | | X |
| Fourfold rise in complement-fixing antibodies (Ten cases) | 11 | 25 | F | X | | X | | X |
| | 12 | 58 | M | X | | X | | X |
| | 13 | 54 | F | X | | X | X | |
| | 14 | | F | X | | X | | X |
| | 15 | 62 | F | | | X | | X |
| | 16 | 54 | F | X | | X | | X |
| | 17 | | M | | | X | | X |
| | 18 | 21 | M | | | X | | X |
| | 19 | 45 | M | | | X | | X |
| | 20 | 7 | M | | | X | | ? |

*From Miller, Hesser and Tompkins¹⁵

X indicates affirmative; blanks, negative

mon and paralysis was rare in this series,¹⁵ while the majority of findings were due to diffuse cerebral involvement. An important negative finding was the lack of meningismus.

The diagnosis was proved (Table 2) by identification of inclusion bodies and/or antibody elevations at autopsy or biopsy among one sub-group of cases which were all fatal except one. Corresponding to the presence of intranuclear inclusions, rises in herpes simplex virus antibodies were seen in a few cases with long enough survival for antibody to develop.

A characteristic finding in cerebro-spinal fluid was observed (Table 2). Erythrocytes and xanthochromia as well as white blood cells were present in the spinal fluid, not only in fatal cases, but also in patients who recovered. Blood appears in small quantities in the spinal fluid as the result of submeningeal hemorrhagic necrosis.

7. *Overlapping manifestations of alcoholic and inclusion body encephalopathies*

All the clinical findings in this patient could have been due to herpes simplex virus encephalitis, but her social history raises the possibility that alcoholic encephalopathy with superimposed viral disease was present.

Herpes simplex meningoencephalitis and alcoholic encephalopathy may cause diffuse cerebral involvement but certain anatomic regions of the

brain may be focally involved as well, particularly the anatomic and functional complex known as the limbic system. It includes the hippocampus of the temporal lobe, fornix, mammillary body, anterior thalamic nucleus and cingulate gyrus. Pathologic findings in brains of alcoholics are more common in the mammillary body, while in brains affected by herpes simplex encephalitis, lesions predominate in the hippocampus and temporal lobe cortex.¹⁴ There are no specific clinical findings with lesions in the limbic system although behavioral changes and impairment of memory are common.

We may never discover which of the patient's cerebral lesions were due to alcoholism and which to a *Herpesvirus*, but it is very likely that the temporal lobe was involved, not only on the clinical ground already discussed, but on the findings of the second electroencephalogram which demonstrated left temporal lobe spikes.

Pathology of Herpes Simplex Virus Meningoencephalitis*

The gross neuropathology of herpes simplex virus meningoencephalitis is submeningeal cortical necrosis and hemorrhage (Figure 1). Leakage of blood from this site into the spinal fluid is accompanied by hemorrhagic as well as inflammatory involvement of the meninges themselves, account-

*From cases investigated by N. Malamud, M.D., Laboratory of Neuropathology at the Langley Porter Institute.

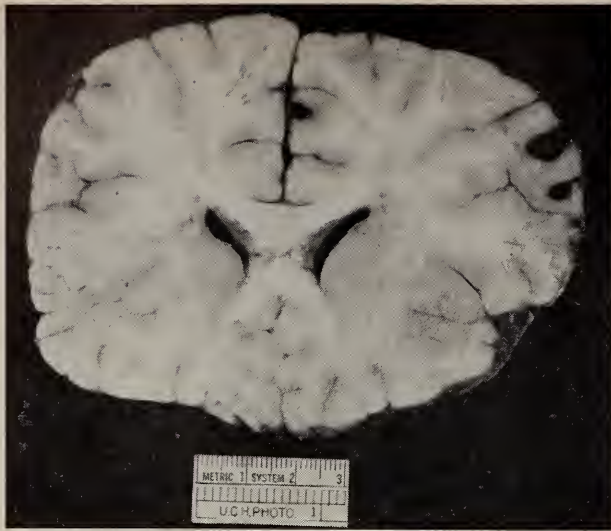


Figure 1.—Gross pathologic changes. There are three areas of hemorrhage and necrosis of cortical grey matter in sites underlying the meninges.

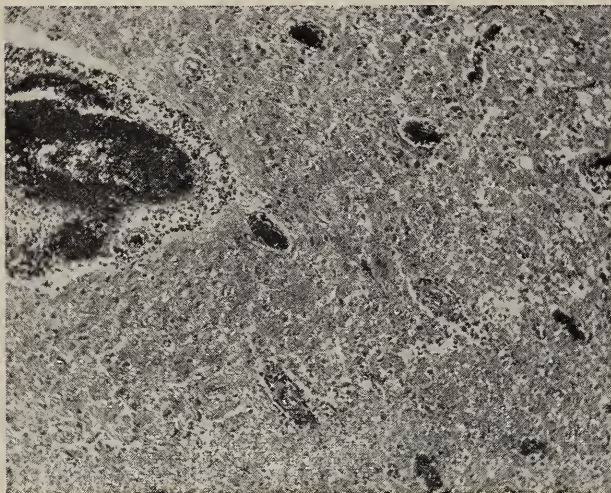


Figure 2.—Microscopic pathologic changes. A large vessel in the meninges (upper left) and smaller blood vessels in the cortex are surrounded by an edematous stroma and inflammatory cells. The walls of the vessels are invaded by inflammatory cells resulting in a necrotizing process and hemorrhage ($\times 100$).

ing for red cells and leukocytes in the spinal fluid as well as xanthochromia. Acute gross necrosis of portions of the temporal lobe (not shown in Figure 1) are related to the personality disorders characteristic of herpes simplex virus meningoencephalitis.

Microscopic features of this disease are perivascular infiltration with lymphocytes, congestion, edema and loss of neurons (Figure 2). In tissue fixed with formalin and stained with hematoxylin and eosin, inclusion bodies may be recognized in neurons and in glial cells as large reddish (eosinophilic) masses with a surrounding halo of clarity in nuclei having margined chromatin

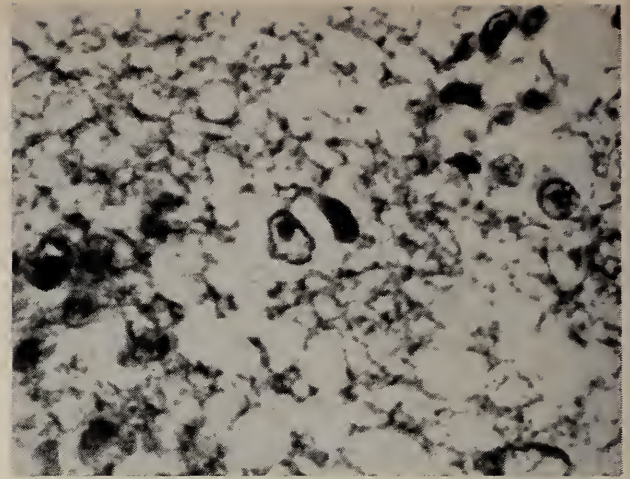


Figure 3.—Herpes simplex virus inclusion body. In the center of the field (and also in the upper right) is a nucleus of a nerve cell in which chromatin forms a dark marginal ring. The dark mass within the ring is an eosinophilic inclusion body. The inclusion body is separated from the margined chromatin by a clear zone ($\times 1400$).

(Figure 3). The inclusion represents a late stage of development of *Herpesviruses* in infected cells.

The Herpesvirus Group

For most of us, the familiar member of the *Herpesvirus* group is herpes virus Type A, or herpes simplex virus, the cause of primary herpetic gingivostomatitis, recurrent herpetic lesions of the mucocutaneous borders of the lip ("cold sore") and of the genitalia and skin, acute and occasionally recurrent herpetic keratitis, herpes simplex virus meningoencephalitis and Kaposi's varicelliform eruption. Encephalitis related to the bite of monkeys has been identified with herpes virus Type B. Unity among (a) herpes simplex virus, (b) the virus of chicken pox and herpes zoster, (c) the cytomegalic inclusion disease virus and (d) the B virus as well as members of the group which occur in animals other than monkeys has been recognized on many grounds and has led to their designation as the *Herpesvirus* group.

1. Virus-cell relationships

The members of this group are desoxyribose nucleic acid (DNA) viruses which initiate viral DNA formation in the cell nucleus. The assembly of the DNA-capsid complex is inhibited by interferon. Growth of viruses of this group is inhibited by halogenated deoxyuridine ribosides (iodouridine deoxyriboside and bromouridine deoxyriboside—IUDR and BUDR) which is incorporated in substitution for thymine in forming DNA, with the



Figure 4.—Primary gingivostomatitis. The buccal mucosa, gums and tongue are involved in a vesiculating eruption with vascular congestion and edema.

result that defective noninfectious virus particles are formed, often lacking the nucleoid. Treatment with IUDR is effective against cellular as well as viral DNA synthesis. For this reason IUDR is used only topically in treatment of herpetic lesions. Fortunately, viral DNA synthesis is continuous while cellular DNA synthesis is discontinuous. Thus, only a few normal cells are killed but most of the virus growing in cells already lethally infected may be inhibited. Unfortunately, production of infectious virus is not stopped completely and inhibition is lost when application of IUDR is discontinued on corneal or skin lesions. IUDR is, therefore, a suppressive agent but significant clinical benefit results from its use in herpes simplex virus keratitis.

Under normal conditions of viral growth, DNA cores or nucleoids are formed in cell nuclei where the cores then acquire structurally complex protein capsids before moving to the cytoplasm. Viral particles at this stage may be spontaneously defective by failure to contain a nucleoid inside the capsid. Particles are "naked" but infectious at this point, but in moving from nucleus to cytoplasm they acquire a protein envelope and are then "enveloped." In the case of cytomegalic inclusion disease virus and varicella-zoster virus, free virus cannot be discovered extracellularly. Herpes simplex passes from cells into extracellular spaces



Figure 5.—Primary herpes simplex infection. In addition to buccal and lip lesions, clusters of vesicles are present in a segmental distribution mimicking herpes zoster. Herpes simplex virus was isolated from these vesicles.

and is capable of extracellular dissemination in the absence of neutralizing antibody.

2. Primary herpes simplex virus infection

The first step in the course of acquaintance with herpes simplex virus usually occurs between six and 36 months of age when passively transferred maternal antibody is absent. Involvement of the lips, gums and tip of the tongue occur in herpetic gingivostomatitis which is the common primary disease (Figure 4). Skin lesions on the face and elsewhere are also characteristic of the initial episode of infection (Figure 5) as is herpetic keratitis.

I am indebted to Dr. Chandler Dawson for illustrations of herpetic keratitis.⁴ The characteristic lesion is known as dendritic because of the branching pattern of corneal involvement (Figure 6). The lesion can be seen when eosin has stained the areas in which epithelium has been destroyed—a contribution that Dr. Samuel Kimura made to recognition of corneal lesions. This pattern can extend to further involvement of the corneal epithelium or to the corneal stroma. Perforation of the cornea may occur at this time. The risk of perforation is



Figure 6.—Herpes simplex keratitis. Eosin has stained a fine, branching linear pattern of epithelial destruction which crosses the pupil and extends in a mottled fashion to portions of the cornea overlying the iris. Note pericorneal vascular congestion.

increased by topical application of corticosteroids in herpes simplex virus keratitis.

In skin vesicles the vesicle fluid elevates and separates the base of the epidermis from the dermis, which is thickened by inflammatory cells, congested vessels and edema. The vesicle fluid is composed of cellular debris, polymorphonuclear leukocytes and very large ("giant") mononuclear cells with lobated or multiple nuclei. Typical cells may be seen in Giemsa-stained smears of scrapings from the base of herpes simplex, varicella and zoster vesicles (Figure 7), and similar cells are present in urine and saliva of patients shedding cytomegalovirus.

Occasionally, the differential diagnosis of a vesicular exanthem includes both a *Herpesvirus* and one of the *Poxviruses* (smallpox, cow pox). The distinguishing cytologic features by which they may be separated are multinucleate giant cells or the cell shown in Figure 7, since this type of cell does not occur in *Poxvirus* vesicles.¹

Generalized herpes simplex virus infection usually occurs in infants and, when fatal, leads to discovery of virus in most viscera and in brain. This fact, associated with additional data, led Miller, Hesser and Tompkins¹⁵ to conclude that all herpes simplex virus meningoencephalitis is part of a primary infection. Alternative interpretations are discussed below.

3. Reactivation of latest *Herpesvirus* infection

Persistence of viruses of this group may occur for a lifetime with episodic recurrence of lesions

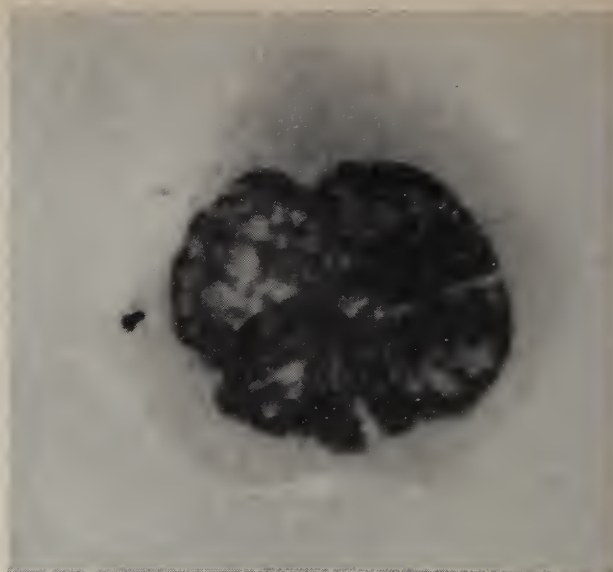


Figure 7.—Herpesvirus giant cell. The nuclear component of this giant cell is either deeply folded or multiple ($\times 900$). In giemsa-stained preparations the nucleus is reddish purple and the cytoplasm is finely granular and blue; these features suggest that it is a cell of reticuloendothelial origin.

or shedding of virus. Herpes zoster probably represents recurrence of latent infection with the zoster-varicella virus; localization of virus in sensory ganglia of the spinal cord or cranial nerves may account for the nerve segment distribution of vesicles. This involves a hypothesis regarding latent neural infection which will be discussed in connection with recurrent herpes simplex.

Recrudescence of latent herpes simplex virus infection occurs in no particular relationship to circulating antibodies among supposed immune persons and is activated by fever, hypersensitivity, sunlight, menstruation, emotional stress or by the cutting of the sensory roots of the fifth cranial nerve. Reactivation of cytomegalovirus has been recognized in adults in the course of management of some renal transplant patients who have been receiving vigorous immunosuppressive therapy and have succumbed to pneumonia in which cytomegalovirus has been identified along with other potential pathogens.

These features of the *Herpesviruses* indicate that activation in latently infected cells is not influenced by circulating antibody but may occur upon immune suppression. Initiation of primary herpes simplex virus infection in infants may be suppressed by passive antibody. Reactivation occurring in the presence of antibody requires that virus (a) be resident but inactive (that is, latent) in all the cells which participate in the recurrent

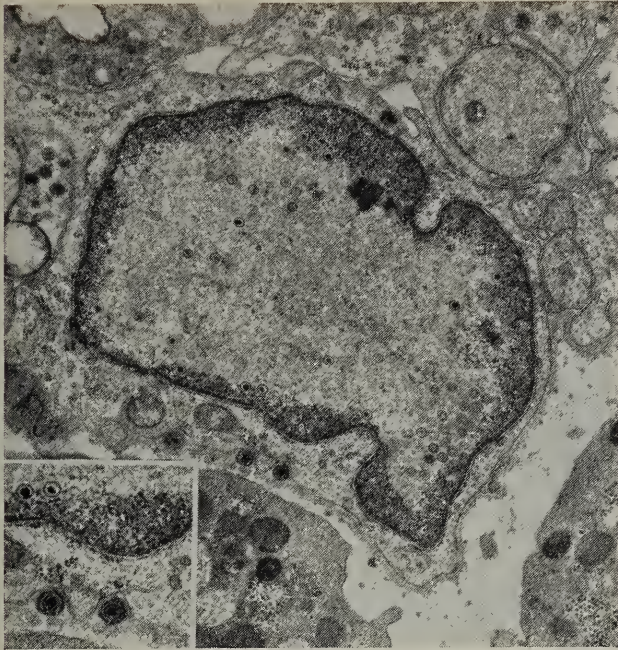


Figure 8.—Electron micrograph ($\times 8000$). A Schwann cell nucleus with marginated chromatin occupies the center of the field. At the lower edge of the nucleus as well as elsewhere throughout the nucleus are “naked” viral particles containing a nucleoid and a single coat of protein, the capsid. Below these two particles and lying just outside the nuclear membrane are two particles bearing a second membrane, the envelope. These details are magnified ($\times 25,000$) in the inset, lower left.

lesions or, in the course of forming a lesion, (b) be passed from infected to noninfected cells by a route other than across extracellular spaces or (c) be passed extracellularly as a particle not susceptible to neutralization.

4. Site of latent infection with herpes simplex virus

Spread of herpes simplex virus from peripheral sites to the central nervous system via nerves was described in 1923 by Goodpasture and Teague⁸ and in 1964 by Johnson.¹¹ The presence of virus particles in Schwann cells of corneal nerves has been recently described by Dawson, Togni and Thygeson of U.C. Medical Center, San Francisco.⁴ A Schwann cell nucleus (Figure 8) contains nucleoid-capsid complexes while enveloped particles appear just outside the cell membrane, indicating the Schwann cells can produce complete virus and suggesting that the mode of movement of virus along nerves may be via Schwann cells.

Paine¹⁴ reviewed the status of neural infection and synthesized, from extensive human and animal data, proposals arising mainly out of the observations of Goodpasture, Cushing³ and Carton.² The latter two observers noted that sectioning the posterior root while the peripheral branches of the fifth cranial nerve were intact in treatment of trigeminal neuralgia resulted in herpes simplex le-

sions at sites innervated by the second and third division of the nerve. If the fifth nerve ganglion was destroyed by injecting a sclerosing agent, or if the peripheral branches were interrupted before sectioning the posterior root, no such lesions occurred.

Paine proposed that infection initiated in the mouth, lips and cornea could pass along the sensory branches of the fifth cranial nerve to the trigeminal ganglion via Schwann cells. Infection could pass beyond the ganglion to involve the nearby pons and medulla and other areas of brain in primary disseminating infection with resultant meningoencephalitis, or remain latent in the ganglion and in the brain. Activation of latent infection in the ganglion was supposed to lead to movement of virus via axons from the ganglion toward the lip to induce lesions of recurrent herpes simplex. Although many observers hold the view that recurrent skin lesions arise from latent infection of the basal cells of the epidermis, arguments favoring latent infection of neural tissues as the basis for recurrent skin lesions and for meningoencephalitis are plausible.

Data reviewed by Leider and coworkers¹² suggest that meningoencephalitis may occur upon activation of latent infection and not only during primary infection. Animal data show that latent infection can be produced in brain and activated by stress.¹⁶ The possibility that herpes simplex virus meningoencephalitis is part of a primary infection is not excluded by such proposal; instead the pathogenesis of herpes simplex virus meningoencephalitis (and of other *Herpesvirus* infections) may be regarded as broad enough to include both primary and reactivated latent infection as the basis of neural and ectodermal lesions.

Paine's review includes a Biblical citation expressing his respect for the versatility and latency of the *Herpesviruses* by likening them to other small but powerful creatures.

“There be four things which are little upon the Earth but they are exceeding wise.

The ants are people not grown, yet they prepare meat in the summer.

The conies are but a feeble folk, yet make their houses in the rocks.

Locusts have no king yet they go forth all of them by bands.

The spider taketh hold with her hands and is in kings' palaces.”

(Proverbs 30:24-28)

DR. CLINE^{*3}: Do the lesions of herpes simplex meningoencephalitis produce localizing findings because of edema and inflammation or by virtue of actual destruction of brain tissue?

DR. CROCKER: The latter accounts for localizing findings. The lesions can be remarkably like abscesses because they result from a necrotizing, hemorrhagic process.

DR. SMITH^{*4}: What specifically should the practicing physician do when he is faced with one of these problems of encephalitis of unknown origin? What measures and what help can he get from the State Department of Public Health?

DR. CROCKER: The State Health Department is very effective in helping to make virological diagnoses by any means, including isolation of viruses from specimens they may consider appropriate, serologic testing of sera obtained at appropriate times in an illness, and by consulting with the physician in determining which viruses should be considered on epidemiologic grounds, such as season of the year and current level of incidence of a given virus infection. The physician is best aided if he telephones the Virus and Rickettsial Diseases Laboratory, State Department of Health, Berkeley, describes the situation and asks advice. Members of the staff there may suggest that stool, spinal fluid or vesicle fluid specimens be submitted and that serum be obtained immediately as well as in two to three weeks to detect changing antibody levels. I have never failed to find assistance of this kind nor have any of our house staff.

DR. SMITH: What is the basis for changes in the glucose content of cerebrospinal fluid? Does bacterial metabolism cause this?

DR. CROCKER: Carrier transport mechanisms are responsible for movement of glucose into and out of the spinal fluid, while bulk flow of fluid via the arachnoidal veins and metabolism of glucose by central nervous system tissue also remove glucose. The net effect leads to maintenance of a lower level of glucose in spinal fluid than in blood in normal persons.⁶ Studies of metabolism of sugar by bacteria, fungi or blood leukocytes have failed to account entirely for the low spinal fluid sugar in pyogenic infections, although some metabolic use of sugar does occur. Altered transport mechanisms are probably involved but the details are poorly

understood, as is the reason for the difference between viral and pyogenic infections with respect to concentrations of sugar in spinal fluid.

ACKNOWLEDGMENTS:

Figures 1, 2 and 3 were provided by Nathan Malamud, M.D., Laboratory of Neuropathology, Langley Porter Institute, University of California Medical Center, San Francisco.

Figures 4, 5 and 6 were provided by Sidney J. Sussman, M.D., Department of Pediatrics, University of California School of Medicine, San Francisco.

Figure 7 was provided by Chandler R. Dawson, M.D., Department of Ophthalmology and the Proctor Foundation for Research in Ophthalmology, University of California Medical Center, San Francisco.

Figure 8 was provided by Phillips Thygeson, M.D., Director of the Proctor Foundation for Research in Ophthalmology, University of California Medical Center, San Francisco.

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California Medicine

EDITORIAL

The Shaping of Medicine's Future

WE WERE IN PRESS before we could know anything of what was said and done at the Western Regional Conference on Future Directions and Decisions in Medical Care, which was held November 10 to 12, but we firmly agree with Dr. John G. Morrison, president of the California Medical Association, who said of this meeting of leaders of the medical profession that it is "one of the most challenging opportunities ever presented to the health care professions to plan for and to provide comprehensive health care services to the public."

The conference, which was organized by the California Medical Education and Research Foundation, was billed as "regional" but it is safe to predict that it is only the first of many of its kind, for the topics of discussion deal with questions that are of vital concern to the medical profession and allied health care personnel under Public Law 89-479—the "partnership for health" law for promoting comprehensive health planning.

At the conference, outstandingly able and well-informed leaders in the ways and means of providing health care were gathered at Chandler, Arizona,

to participate in panels and workshops on "Goals and Objectives of the Medical Profession," "The Components of Comprehensive Health Planning and the Coordination of Services and Facilities," "Relationship of Federal, State and Local Governments to PL 89-749" and "Analysis and Evaluation of Planning Processes, Based upon Previous Experiences and Expectations of PL 89-749."

Most of the participants were from the Western United States, although some of the speakers were officials of interested departments of the Federal Government, and there were also representatives of the American Medical Association in attendance.

That the conference was "regional" rather than national in scope was largely because the idea for such a meeting found ready acceptance among leaders in the CMA when Dr. James Wharton of the U.S. Public Health Service proposed it to them in 1966. Their thoughts already had been turning to just such questions, and the answers already were being sought through the searching studies of the association's Bureau of Research and the work of the Commission on Community Health Services, the Committee on the Role of Medicine in Society, the Commission on Allied Health Professions and others. Dr. James C. MacLaggan, then president of the CMA, grasped the opportunity to hold a comprehensive meeting for a broad give-and-take of information and formulation of thought. Murray Klutch, the association's director of research, set about financing and planning the conference and Dr. Morrison, who succeeded to the presidency of CMA during the organizational stage, gave con-

tinuing enthusiastic support to the project. After a grant was obtained by CMERF from the Public Health Service of the Department of Health, Education, and Welfare, a program was drawn up and outstanding persons of vision and practical experience were enlisted as discussants. The program also made provision for a large attendance by persons who were not to be active participants but who wished to be present as observers and reporters.

As we began by saying, we cannot know at this writing any of the details of what the meeting brought forth. We do know, however, that the fact that such a meeting was held is of resounding importance. The thought processes given impetus there will play a large part in shaping the changes in medicine that are taking place now and that are yet to come.

Not to Take a Total Loss

OUR WARM GOOD WISHES go with William Whelan as he leaves the employ of the California Medical Association to become executive director of the California Hospital Association. In his almost ten years of service with CMA, Bill Whelan showed himself to be not only an outstanding general executive but to have extraordinary capabilities in the fields of medical socio-economics, legislation and governmental relations. In his job he brought together steadfastness to essential purpose, thorough realism in negotiation and a willingness to work as hard and as long as the interests of this medical association demanded.

These attributes and the excellent personal relations he has with all persons with whom he deals will now be turned primarily to the purposes of the California Hospital Association. Even so, we retain residual benefits from his years with us. And while we acknowledge a loss at Bill's departure, we believe that he carries with him an understanding and feeling of good will that cannot but further improve the good relationship that has developed between the CMA and the CHA in recent years.

We congratulate both the California Hospital Association and its new executive director.

Veterinary Research

IT IS QUITE regrettable that the excellent symposium on research by veterinarians* presented in Los Angeles occurred on a Saturday just before the annual meeting of the California Medical Association, when few physicians and few veterinarians could attend. The reported research was of a high order and provided much information which should be useful to physicians as well as to veterinarians, for there are many common denominators in human and animal medicine.

It was especially important to note some of the advantages of the veterinarian in experimentation. Animals are commonly used by physicians in contrived studies in which infection or injury are deliberately inflicted, in order to study a given phenomenon in the hope that information thus derived can be applied to human disease. The veterinarian, in addition to this experimental method, encounters experiments in nature in which he can follow disease, injury or genetic defects as they occur spontaneously.

Veterinarian experimental medicine has still other great advantages: Blood lines are usually known most exactly; information need not be obtained, as in human disease, from the usually inaccurately reported family history. The experimenter can breed patients selectively for the production of genetic alteration, heterozygotes or homozygotes as he may choose. He may not have to wait for his patient to die for he can determine the precise state at which to interrupt progress and obtain autopsy information. Informed consent is not necessary for the use of new therapy.

As there are many similarities between human and animal diseases and many common problems and concepts, the close association of the two new schools of medicine in California (Davis and Irvine) with schools of veterinary medicine will provide opportunities to both disciplines.

EDWARD B. SHAW, M.D.

*One of the three articles, Rabies—Suggested Indications for Treatment of Exposed Persons, appears in this issue, beginning on page 363. The other two will appear in succeeding issues.



California Medical Association

NOTICES AND REPORTS

Council Meeting Minutes

536th Meeting

Tentative Draft: 536th Meeting of the Council, San Francisco, Hilton Inn, 26 August 1967.

The meeting was called to order by Chairman Miller at the Hilton Inn, on Saturday, 26 August 1967, at 9:30 a.m.

A quorum was present and acting (full roll call, including names of invited guests, appears in item 34).

1. Minutes for Approval

The minutes of the 534th and 535th Meetings of the Council, held 8 July and 2 August respectively, were approved as distributed.

JOHN G. MORRISON, M.D. President
MALCOLM C. TODD, M.D. President-Elect
WILLIAM F. QUINN, M.D. Speaker
JOSEPH F. BOYLE, M.D. Vice-Speaker
ALBERT G. MILLER, M.D. Chairman of the Council
HAROLD KAY, M.D. Vice-Chairman of the Council
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2. California Medicine Appointments

On nominations duly made and seconded, the following were unanimously appointed to the positions shown (to become effective 1 January 1968):

Editor of CALIFORNIA MEDICINE: Malcolm S. M. Watts, M.D.

Associate Editor of CALIFORNIA MEDICINE: Lloyd H. Smith, Jr., M.D.

The nominating committee (composed of current Editor Dwight L. Wilbur, M.D. and the Committee for Emergency Action) was authorized to work out new financial arrangements for the appointees.

3. AMA Activities

In the absence of AMA President-Elect Dwight L. Wilbur and AMA Board member Burt L. Davis, Chairman Miller called on Mr. Jerry Gould of the AMA Field Service, to report on current AMA activities and concerns. Mr. Gould stated that the recent AMA Communications Institute had been most successful and expressed his pleasure at the CMA representation. Mr. Gould also commented briefly on the Senate Finance Committee hearings on H. R. 12080 (Social Security Amendments of 1967).

4. Report of the President

President Morrison previewed the meetings with Northern California society presidents to be held in conjunction with this meeting of the CMA Council.

Doctor Morrison also reported on the progress of the ad hoc Committee on Osteopathy recently

established by the Council. Another major subject which Doctor Morrison discussed was the Workmen's Compensation Fee Schedule. He stated that he had recently met with the Medical Advisory Committee to the Industrial Accident Commission. At this meeting, the concept of applying "usual and customary" fees was again discussed and received thoughtful consideration.

5. *CMERF Criteria for Acceptance of Funds*

On behalf of the Board of Directors of the California Medical Education and Research Foundation, President Morrison presented a "Statement on the Rationale and Criteria for Acceptance of Funds." There was some discussion regarding a possible addition to the statement which would indicate that CMERF would keep in mind the ultimate disposition of study results when accepting funds from outside sources. It was suggested that the statement be accepted, with the stipulation that CMERF would submit an additional statement at the next meeting of the Council.

ACTION: *Voted to accept CMERF Statement on "Rationale and Criteria for Acceptance of Funds" (appended) and to ask CMERF to submit an additional statement regarding disposition of studies financed by outside sources.*

6. *Report of the President-Elect*

President-Elect Todd reported on several meetings he had attended since the last meeting of the Council. He stated that his recent attendance at a Board meeting of the California Hospital Association served to reinforce his confidence in cooperative efforts by CHA and CMA. Doctor Todd also commented on the Annual Meeting of the Audio-Digest Foundation, stating that the organization continues to be a dynamic one of which CMA can be extremely proud. Regarding the AMA Communications Institute, Doctor Todd reported that both he and Doctor James MacLaggan had attended this meeting as well as the meeting of the Association of State Medical Association Presidents. He said that other states continue to look to California for leadership, especially regarding the complex problems posed by Title 19 of Medicare. The basic thread running throughout these meetings, said Doctor Todd, was the need for greater involvement and understanding on the part of the individual physician members.

7. *Committee on Committees' Recommendations*

On behalf of the Committee on Committees,

President-Elect Todd made a number of recommendations and stated that the Committee was most pleased to have Mrs. Betty Schallenger working with it. Chairman Miller, on nominations presented by the Committee on Committees and the Council concurring, made the following appointments:

Task Force on P.L. 89-749—Malcolm C. Todd, M.D., Long Beach, chairman; James C. MacLaggan, M.D., San Diego; William F. Kaiser, M.D., Berkeley; Arthur F. Howard, M.D., Fresno; James C. Malcolm, M.D., Oakland; Albert G. Clark, M.D., San Francisco; Jean F. Crum, M.D., Downey; Frank C. Melone, M.D., Ontario; James H. Yant, M.D., Sacramento; and Stanley A. Skillicorn, M.D., San Jose.

The Council approved the recommendations that this Task Force be limited to ten persons and that at its first meeting, the group should define the scope of the Task Force and develop a budget.

Commission on Community Health Services—James H. Yant, M.D., Sacramento, as chairman (replacing Harold Kay, M.D., who resigned as chairman and as a member of the Commission).

Scientific Board—James L. Goebel, M.D., San Rafael, as a member (replacing Robert J. Prentiss, M.D.).

Committee on Nominations of the Scientific Board—Edmund L. Keeney, M.D., La Jolla, as a member (replacing Robert J. Prentiss, M.D.).

Ad hoc Committee to Study Standardization of Hospital Medical Records—Joseph W. Telford, M.D., San Diego (chairman); William L. Argo, M.D., Fresno; Arthur H. Rice, M.D., Berkeley; Albert E. Warrens, M.D., Chico.

Committee on Drugs and Subcommittee on Adverse Drug Reactions—Samuel Woolington, M.D., Long Beach, as a member.

Doctor Todd also recommended that the Council authorize President Morrison to invite presidents of component medical societies as well as presidents of districts of Los Angeles County Medical Association to attend, or submit the name of an alternate to attend, the Western Conference on Future Directions and Decisions in Medical Care, to be held in Chandler, Arizona, November 10 to 12, 1967.

ACTION: *Voted to approve the above request for authorization.*

The final recommendation of the Committee on Committees was that a letter from Lewis T. Bul-

lock, M.D., regarding health education in schools, be referred to the Committee on School and College Health. There was discussion, during which Doctor Bullock expressed his firm belief that CMA should do much more in the field of health education, and that the name of the committee charged with this responsibility should reflect its concern with health education.

ACTION: *Voted to refer Doctor Bullock's letter and thinking regarding an expanded CMA role in health education to the Committee on School and College Health.*

8. Medi-Cal Adjustments

Following discussion initiated by President Morison regarding the need for CMA to issue a public statement regarding the proposed emergency regulations for the Medi-Cal program, the Council considered a statement embodying the following major points:

(a) The CMA accepts the appraisal and conclusions of the administrator of the Health and Welfare Agency in regard to the fiscal problems of the program.

(b) The CMA agrees that the proposed emergency regulations appear to be a feasible approach to the problem.

(c) CMA's fundamental concern is with the provision of quality medical care for all.

(d) The CMA pledges its cooperation with the state administration and the Health and Welfare administrator, to continue to provide the best care possible under the program.

ACTION: *Voted to authorize the Committee for Emergency Action to develop a public statement regarding current emergency measures to curtail Medi-Cal costs, using the above as guidelines.*

After the statement was adopted by the Council, Mr. Williams spoke briefly, expressing his appreciation for CMA cooperation and reassuring the Council that the administration would work to improve the program and protect the concept of mainstream care.

ACTION: *Voted to urge component medical societies to develop comprehensive and realistic review mechanisms that would contribute to the future fiscal soundness of the Medi-Cal program.*

9. UC Medical School at Davis

Dean John Tupper of UC Medical School at Davis reported on progress at his growing school, stating that its faculty now numbers 24 members.

Doctor Tupper introduced the school's recently appointed assistant dean and head of the Department of Pathology, Doctor Robert Stowell, formerly scientific director for the Armed Forces Institute of Pathology.

10. State Department of Public Health

Doctor Robert Day of the State Department of Public Health briefly discussed some developments regarding Public Law 89-749, stating that the California Conference of Local Health Officers would be holding a special meeting on the subject on 30 August.

Doctor Day also reminded the Council that a report from the Surgeon General on influenza had recently been issued. Doctor Day said that the report would seem to indicate that while there may be a major outbreak of influenza in the eastern part of the nation, California will probably not be affected to a great extent. However, he said, immunization is recommended for those in "high susceptibility" groups.

He also touched upon and praised the cooperative projects with several county medical societies to provide health services to agricultural migrants and their dependents.

Finally, Doctor Day pointed to recent developments regarding environmental health in the state. It was hoped, he said, that the creation of two new entities—an Air Resources Board and a Water Resources Board—would enable the state to take greater and better coordinated action in these areas.

11. State Department of Mental Hygiene

Doctor James V. Lowry, director of the State Department of Mental Hygiene, distributed to the Council a chart which showed that population in state hospitals for the mentally ill has dropped consistently since 1962. He pointed out that the state started this year with some 4,500 fewer patients than at the start of the 1965-66 year. Doctor Lowry stated that funds are available to maintain a staffing level proportionate to the level which existed in July 1966.

12. State Department of Social Welfare

Doctor John T. Skelly of the State Department of Social Welfare, described a "top priority" project aimed at getting as many people as possible off the welfare rolls and into employment. He said that increased attention will be given to medical evaluation for employability, naming four major

categories of employability. Doctor Skelly said that the success of the plan would depend in part on obtaining the services and advice of physicians who would conduct examinations similar to pre-placement physical examinations for industrial organizations. He said that the Department of Social Welfare seeks the cooperation and support of CMA, local medical societies, the State Department of Vocational Rehabilitation and the State Department of Employment in carrying out this project.

13. *State Department of Rehabilitation*

Doctor Richard Young of the State Department of Rehabilitation said it gave him great pleasure to announce that the Medical Advisory Committee to the Department is to be expanded and reactivated.

Doctor Young also reported on a regrouping of services in the U.S. Department of Health, Education and Welfare, in that the former head of the Vocational Rehabilitation Administration has been given a new job as administrator of the Social Rehabilitation Service Unit of HEW.

14. *Social Security Administration*

Mr. Thomas N. Saunders of the Bureau of Health Insurance, Social Security Administration, reported that a new policy decision now makes it possible for patients in extended care facilities to receive benefits of diagnostic services by independent laboratories under Medicare. Mr. Saunders also commented on the HEW meeting on Utilization Review in Hospitals and Extended Care Facilities, to be held 29 August in San Francisco. He stated that expenditures for extended care services under Medicare may be as much as 10 times the figure originally estimated and that this subject will receive special attention at the meeting.

15. *Assistant Surgeon General*

Doctor R. Leslie Smith, who was recently appointed Assistant Surgeon General for the U.S. Department of Health, Education and Welfare, reported that he had talked at length to the Medical Executives Conference regarding P.L. 89-749 the previous day. Doctor Smith said that he would make copies of his presentation available for distribution to the Council.

16. *California Nurses' Association*

Mrs. Helen Hancock, president, commented on

joint projects of CNA and CMA and introduced Edna J. Brandt, president-elect of the California Nurses' Association.

17. *California Medical Assistants Association*

Miss Helen Goldman, president of the CMAA, thanked CMA and AMA for their assistance in promoting the 11th Annual Convention of the American Association of Medical Assistants, to be held October 11 to 15 at the International Hotel in Los Angeles.

18. *Governor's Survey on Efficiency and Cost Control*

Doctor Carl E. Anderson, member of one of the teams which have been conducting the Governor's Survey on Efficiency and Cost Control, reported that his group, which has been evaluating the operations of the State Department of Public Health, had submitted its preliminary and unedited report. He said that the governor plans to release the reports early in October, if possible. Doctor Anderson expressed the hope that CMA would utilize the reports pertaining to medicine as a basis for in-depth discussion.

Doctor Anderson said he could not discuss the reports until their release, but he did want to make two points in relation to CMA activity in the area of public health. First, he stressed, CMA needs to establish more realistic and effective liaison with all segments of state government that influence medicine. Second, he said, that medicine needs to strengthen its image as the basic instrument which influences public health.

19. *Bureau of Research and Planning*

Bureau Chairman Carl Anderson directed the Council's attention to a written report reviewing current research activities. On behalf of the Bureau, he asked Council authorization to distribute the recently compiled "Reference Book on Selected Health Manpower Data" to component societies, medical schools and other organizations concerned with health manpower, continuing medical education and comprehensive health planning.

ACTION: *Voted to authorize distribution of the reference book as requested.*

20. *Finance Committee*

Finance Committee Chairman Harold Kay submitted for Council approval a clarification of the policy on honorariums for any CMA member under

exceptional circumstances. When approved, he said, the statement would be incorporated in a letter explaining CMA honorarium policy as well as procedures for preparation of expense vouchers.

ACTION: *Voted to approve the policy of \$200 per day maximum be paid to any member of CMA for a full day away from practice while covering special assignment projects upon authorization from the Finance Committee.*

Doctor Kay also presented recommendations concerning the amount of honorarium per day to be incorporated in the contract with the State Department of Public Health for services of CMA Medical Staff Survey Teams.

ACTION: *Voted to authorize an honorarium of \$100 per day (over and above the per diem allowance of \$65 for travel expense and \$18 maximum for room and board allowed by the state) to be paid to CMA members serving on a contractual basis in conducting medical staff surveys for the State Department of Public Health.*

Another recommendation of the Finance Committee was that the Group Life Insurance Program provided for CMA Staff be modified so that the coverage would extend beyond age 65 for eligible persons. With the extension, coverage would be reduced each year after the employee reaches age 65 until it reached 50 per cent, where it would remain constant. Doctor Kay said that the additional cost to CMA would be about \$1,000 per retired employee per year.

ACTION: *Voted to approve the extension of life insurance coverage for CMA employees after they reach age 65.*

As a final recommendation, the Finance Committee asked Council approval to increase the annual contribution to the California State Chamber of Commerce from \$1,500 to \$2,000 per year.

ACTION: *Voted to approve the increased yearly contribution to the California State Chamber of Commerce.*

In conjunction with the Finance Committee report, two documents were distributed to the Council—one showing the growth of the CMA from 1948 to 1967; the other, a financial statement for the CMA and its Board of Trustees.

21. Commission on Community Health Services

Outgoing Chairman Harold Kay recommended on behalf of the Commission that the Council endorse a required performance evaluation program for clinical laboratories as an effective means for

clinical laboratory improvement. Doctor Kay said that such a required performance evaluation program was proposed by the California Society of Pathologists and that the Division on Laboratories of the State Department of Public Health has had the authority to implement such a program (Section 1226, Business and Professions Code) since 1939. After lengthy discussion, which included a presentation by Mr. Miles Snyder, executive secretary of the California Society of Pathologists, the Council made the following decisions:

ACTION: *Voted to commend the California Society of Pathologists and other specialty organizations for their efforts conducted on a voluntary basis to improve continuously the quality of medical care and to encourage these organizations to continue and expand their voluntary actions.*

ACTION: *Voted to request the Council chairman to charge an appropriate committee of the Council to bring to the 30 September meeting an evaluation of this question relative to potential interference in the area of clinical laboratory practice of medicine by a state agency through a mechanism developed under the Medicare program.*

Doctor Kay also reported on a recent meeting with representatives of the two dental associations in the state on the subject of fluoridation. He said that a state-wide fluoridation campaign was being considered and the CMA had been asked to express its willingness to participate in such an effort. Although he did not ask for approval of a specified CMA monetary contribution to the campaign, Doctor Kay stated that the Council should realize that it would probably entail an allocation of \$15,000 to \$25,000 by the CMA if the campaign were carried out as planned.

ACTION: *Voted to proceed with plans to participate in the state-wide fluoridation campaign.*

Doctor Kay reminded the Council about two upcoming CMA-sponsored meetings: a Conference on Emergency Medical Services and Disaster Preparedness (7 October, San Francisco) and a Conference on Health Manpower Distribution in Rural California (14 October, Los Angeles).

As a final item, Doctor Kay suggested that the CMA appoint a representative to the Advisory Committee to the State Department of Public Health, Division of Laboratories (regarding Laboratory Performance Evaluation Program).

ACTION: *Voted to appoint an official CMA representative to the Advisory Committee on Performance Evaluation Programs of the Division of Laboratories, State Department of Public Health.*

ACTION: *Voted to appoint James Yant, M.D., as CMA representative on the advisory committee.*

Doctor Kay expressed his gratitude for having had the opportunity to serve as chairman of the Commission. On behalf of the Council, Chairman Miller thanked Doctor Kay for his contributions while chairman of the Commission on Community Health Services.

22. *Commission on Allied Health Professions and Services*

Chairman Frank Melone reported that the Health Manpower Council had met on 2 August and had elected the following officers to form its Executive Committee: Chairman, Mr. Richard Highsmith; vice chairman, Mrs. Talcott Bates; secretary, Doctor Albert Clug; treasurer, Doctor Harold Kay; member-at-large, Mr. James T. Adair. He said that the Health Manpower Council now is seeking an executive director.

On behalf of the Committee on Allied Health Personnel and the Commission on Allied Health Professions and Services, Doctor Melone offered a statement on "Utilization of Allied Health Personnel Directly Associated with Patient Care" for Council consideration. Doctor Melone pointed out that the statement had been developed to remind physicians not to use or permit members of the health team to perform tasks beyond the limits of their license and/or certification.

ACTION: *Voted to approve the statement on "Utilization of Allied Health Personnel Directly Associated with Patient Care" (appended).*

23. *Meeting with California Committee of the Health Insurance Council*

Doctor Arthur Howard briefly reported on a meeting of the Commission on Medical Services and the Committee on Insurance and Prepayment with the California Committee of the Health Insurance Council.

Among subjects discussed at the meeting, Doctor Howard said, was the lack of a standardized definition and application of an existing illness clause in medical care insurance. Insurance representatives agreed to submit the problem to the Inter-Company Medical Directors Committee for re-evaluation of underwriting principles, with the suggestion that the assigned risk pool approach be included in the re-evaluation. Doctor Howard said that it was the consensus that California Blue Shield should be encouraged to experiment with

the assigned risk pool concept for individual or small group coverage, to obtain statistics which could be used by the insurance industry.

Doctor Howard said that the group also discussed House of Delegates Resolution No. 60-67, requesting that the health insurance industry be encouraged to develop programs to provide payments for diagnostic procedures on an out-patient basis. Insurance representatives agreed to refer this request to the Inter-Company Medical Directors Committee for reappraisal.

Regarding House of Delegates Resolution No. 65-67 (requesting that a standard reporting form for private and government third party payment programs be designed), Doctor Howard stated that both the National Health Insurance Council and the AMA have been working for some time on developing a new standardized claim form to be used for computer billing services. A proposed form has been approved by the Health Insurance Council and is now in the hands of the AMA Commission on Medical Services.

24. *Committee on Fees*

On behalf of the Committee on Fees, Chairman William H. Thompson reported that the Committee is in the process of an extensive revision of the *Relative Value Studies* (no extensive survey of the relativity of unit values having been made since 1958-59). Doctor Thompson said that a mass of computer data on standard (non-government) programs employing usual and customary fees was now available through California Blue Shield and that CMA's actuarial consultant had assured the committee that this data is statistically valid and would provide a much broader basis for assigning unit values than has been available in the past. Doctor Thompson requested authorization for an expenditure of an estimated \$26,000 to pay for the costs of programming and computer time as well as actuarial consultation.

ACTION: *Voted to authorize the Committee on Fees to expend \$26,000 for an extensive revision of the Relative Value Studies.*

Chairman Thompson and Councilor Pheasant presented a second request—for authorization to aid AMA in developing its revised *Current Procedural Terminology* by providing tentative revisions of sections of the *Relative Value Studies* as they are completed and at the discretion of the committee.

ACTION: *Voted to authorize the Committee on Fees to provide AMA with tentative revisions of sections of the Relative Value Studies as they are completed (at the discretion of the committee).*

25. Report of Legal Counsel

Legal Counsel Howard Hassard first reported on the possible effects on CMA of a proposed federal income tax on revenue from advertising and convention exhibits of tax-exempt organizations. He stated that public hearings on this subject were held in Washington, D.C. late in July and that the Internal Revenue Service now has it under advisement. He reported that the independent accounting firm retained by CMA had been asked to determine the effect on the Association if such taxes were imposed. It was determined that if a tax were imposed on advertising in *California Medicine*, the effect would not be great. If exhibits at CMA's Annual Session were taxed, however, the effect would be substantial. Mr. Hassard concluded this section of his report by saying that the effect on the dues-paying member physician would be felt much more insofar as AMA is concerned. The AMA currently receives well over half of its income from advertising in its official journal.

On the subject of osteopathy, Mr. Hassard reported that a member of the State Legislature had recently asked the Attorney General for an opinion on whether it is somehow unconstitutional for California not to have a licensing provision for osteopaths. CMA's legal counsel was, in turn, asked for its opinion, which was presented to the Attorney General in the form of an extensive brief pointing out that the state has the power to license or not to license in the health field and that the absence of licensure requirements for osteopathy does not violate any constitutional guarantees. Mr. Hassard pointed to this as an example of the continuing pressure concerning reinstatement of osteopathy in California.

Mr. Hassard drew the attention of the Council to AMA's recent Statement on Professional Courtesy.

The last subject covered by Legal Counsel Hassard was the mounting problem of professional liability insurance for physicians. He cited several recent cases in Southern California which showed that the sums being awarded in malpractice cases are mushrooming—thus making the outlook regarding availability of malpractice insurance dimmer. Mr. Hassard pointed out that at least two

legislative interim studies on the problems of malpractice are under way.

26. California Health Data Corporation

Doctor James C. MacLaggan, chairman of the Commission on Hospital Affairs, presented a brief report on progress regarding the California Health Data Corporation, stating that the incorporation papers and bylaws (approved by the CMA Council, 27 May 1967) had been finalized. At the recent meeting, attended by representatives of CMA, the California Hospital Association and the State Department of Public Health, a subcommittee was established to delineate further the role of the California Health Data Corporation, particularly regarding its relationships with other health data gathering organizations.

27. Committee on Legislation

Chairman Dan Kilroy presented a report on legislative activity since the last meeting of the Council, pointing out that the 1967 Session of the Legislature had adjourned 7 August, after 219 days of continuous session. He said that the Committee on Legislation would furnish the Council with a complete analysis of the 1967 Legislature following the "Veto Session" to be held the week of 4 September. Doctor Kilroy called on Mr. Ben Read, who discussed the special election held in San Francisco at which Judge Milton Marks was elected to fill the position formerly held by Senator Eugene McAteer. Mr. Paul Brown was asked to comment on Senate Bill 1065.

28. Medical Executives Conference

Mr. Eldon Geisert, chairman of the Medical Executives Conference, recommended to the Council that a meeting be held as soon as possible to provide an opportunity for CMA executive secretaries and California Blue Shield to discuss new ways to promote cooperation and communication.

ACTION: *Voted to approve the meeting with executive secretaries and California Blue Shield.*

29. Position Paper on Drug Abuse

Doctor William Quinn recommended to the Council that it approve as CMA policy a position paper on drug abuse, developed in cooperation with, and at the suggestion of, the Medical Executives Conference.

ACTION: *Voted to approve the position paper on drug abuse (published in October issue of California Medicine).*

30. *Committee on Organizational Review and Planning*

Chairman Jean Crum summarized discussion on a variety of subjects which had been considered at the 4 August 1967 meeting of the Committee on Organizational Review and Planning. Councilor Crum said that a written summary of the discussion would be distributed to the Council in advance of its next meeting. On behalf of the committee, Doctor Crum recommended to the Council that the *function* of the recently disbanded Committee on Scientific Information be continued in cooperation with the Executive Committee of the Scientific Board, which would designate individuals qualified to make responses to scientific questions in specific areas—on request. Councilor Crum pointed out that Scientific Board Chairman William P. Longmire, Jr., had attended the committee meeting during which this method of continuing the function was formulated.

ACTION: *Voted to approve continuing the function of the Committee on Scientific Information in cooperation with the Executive Committee of the Scientific Board.*

31. *August 29 Meeting on Utilization Review*

Immediate Past President MacLaggan directed the attention of the Council to the written materials in the Council notebooks previewing the 29 August meeting on Utilization Review, sponsored by the U.S. Department of Health, Education and Welfare. He also asked that the Council authorize Councilor William Kaiser to attend the meeting with him.

ACTION: *Voted to authorize Doctor William Kaiser to attend the 29 August HEW meeting on Utilization Review.*

32. *Staff Report*

Executive Director Robert L. Thomas briefly commented on steps that were being taken to define more clearly areas of responsibility within the CMA staff, and said that he hoped to be able to present to the Council at its next meeting a fairly detailed table of staff organization.

Mr. Thomas also discussed the recent administrative survey of Sonoma County Medical Society that had been conducted at the request of the society. The survey team was composed of Mr. Thomas (chairman), Mr. Lytton Hetland, and three county society executive secretaries. The resulting report was well received. Two other

component societies—Marin and Santa Barbara—have requested similar surveys. Mr. Thomas said that he felt this was a valuable service which he was pleased to see CMA provide.

33. *Membership*

Fifteen applicants were voted election to Associate Membership. These were Erich K. Die-mand, Kathleen Anne Malloy, James M. Poynter, Harry Saul Weinstein, Alameda-Contra Costa County; John R. Marron, Monterey County; Armine K. Meghrouni, Orange County; Harold L. Snow, Ralph E. Yost, San Mateo County; Harvey N. Blume, Lois Lowden, Santa Clara County; Edwin Robert Geiger, Jr., Tulare County.

Five members were voted election to Retired Membership. These were: Benjamin H. Pratt, Kings County; John M. Wakefield, Sacramento County; Donald A. Carson, Otto Guttentag, San Francisco County; Vernon Van Zandt, Tulare County.

Reduction of dues was voted for nine members for reasons of prolonged illness or postgraduate education.

34. *Roll Call*

Present were President Morrison, President-Elect Todd, Speaker Quinn, Vice-Speaker Boyle, Secretary Weyrauch, and Councilors Moore, Melone, Eastman, Woolington, Gooel, Pheasant, Bullock, O'Connor, Shapiro, Rogers, Crum, Watson, Maguire, Burnett, Miller, Watts, Fenlon, Kay, Kaiser, Rose, Yant, Grunigen and Immediate Past President MacLaggan.

Present by invitation were CMA staff members Becker, Borgfeldt, Bowman, E. Collins, Curley, Eberlein, Edwards, Goldman, Griffith, Hetland, Klutch, Lemos, Miller, Price, Redfern, Thomas and Whelan; Messrs. Hassard, Huber and Willett, Legal Counsel; Component Society Executives Scheuber of Alameda-Contra Costa, Garrick of Forty First, Lingerfelt of Fresno, Geisert of Kern, Brock of Imperial, Baker of Los Angeles, Sower of Marin, Searcy of Napa, Bannister of Orange, Walters of Riverside, Dochterman of Sacramento, Donmyer of San Bernardino, Nute of San Diego, Thompson of San Joaquin, Wood of San Mateo, Marvin of Santa Barbara, Donovan of Santa Clara, Funk of Solano, Brown of Sonoma and Whitehall of Stanislaus; Messrs. Babb, Clark, Heller and Koch of California Blue Shield; Messrs. Read, Brown and McWilliams of the Public Health

League; Doctors Tupper and Stowell of UC Medical School at Davis; Messrs. Williams, Shumway, Fugina, Stewart and Barnes of the Health and Welfare Agency; Doctor Combs of the State Board of Medical Examiners; Doctor Bost of the State Department of Public Health; Doctor Lowry of the State Department of Mental Hygiene; Doctor Skelly of the State Department of Social Welfare; Doctor Young of the State Department of Rehabilitation; Doctor Radl of the State Department of Employment; Doctor Smith of the U.S. Public Health Service; Mr. Saunders of the Bureau of Health Insurance, Social Security Administration; Mr. Ward of the California Committee on Regional Medical Programs; Mr. Snyder of the California Society of Pathologists; Mr. Gould of the AMA; Mrs. Hancock of the California Nurses' Association; Miss Goldman of the California Medical Assistants Association; Doctors Carl Anderson, R. L. Anderson, Ardell, Clark, Daily, Davis, DeWitte, Elston, Garrett, Gibbons, Holm, Hoskins, Howard, Kilroy, Martin, Morozumi, Schor, Silver, Steinberg, Taugher, Thompson, Wayburn and others.

35. *Adjournment*

The meeting was adjourned on Saturday 26 August at 4:40 p.m.

ALBERT G. MILLER, M.D., *Chairman*
HELEN B. WEYRAUCH, M.D., *Secretary*

Appendix A

Statement on the Rationale and Criteria for Acceptance of Funds by the California Medical Education and Research Foundation

John G. Morrison, M.D., President

The California Medical Education and Research Foundation is a nonprofit, tax-exempt educational and research organization which receives and disburses funds for the purposes of (1) encouraging needed support for medical education and (2) for research into a broad spectrum of social and economic aspects of health care. Both of these broad areas of activity are carried out in the public and professional interest.

The existence of the Foundation reflects the complex demands of a society for ever-expanding health care services and for the application of the products of new medical technology and new scientific discoveries on behalf of the public. The

application and dissemination of such information, as well as the organized quest for a variety of other data and information, frequently involves the expenditures of substantial amounts of money.

Ideally, and whenever feasible, when the medical profession requires large sums of money to support or engage in activities which will aid it in achieving its dual objectives, such funds should be obtained through its own resources. However, occasions do arise when other private resources or public tax funds are the only ones readily available for such purposes. It is, therefore, the policy of the Board of Directors of the California Medical Education and Research Foundation to accept funds from whatever sources it deems most advisable to enable the Foundation to fulfill its stated purposes. Each project or activity for which funds would be sought would be considered on its individual merits.

With respect to Federal public tax funds, it is the policy of the California Medical Education and Research Foundation to apply for, or accept, funds which might not otherwise be easily or readily available from private sources, for programs, projects and activities which, in its considered judgment or that of the California Medical Association Council or that of the House of Delegates:

1. Are considered to be of immediate or long-range concern to the health interests of society, and which
2. Will enable the Foundation to achieve its timely educational and professional objectives.

Approved by the CMA Council 26 August 1967.

Appendix B

Statement on Utilization of Allied Health Personnel Directly Associated with Patient Care

In practicing his profession, the true professional develops skills by learning from those who have had more training and experience. It is only natural that the utilization of these additional skills be exploited so that increased efficiency can be obtained in patient care. Within the concept of rendering care to victims of illnesses or accidents, each of the members of the "health team" has specific duties, abilities and talents. Limitations of care that might be rendered by one or another of the "team" are primarily imposed by law and secondarily imposed by certification, by ability, and by level of training. It is in the best interest of the patient that the best skills of all the health care personnel available be utilized to the fullest.

The people of California have, through the Legislature, established the limits to which they will permit those engaged in patient care to practice their vocation. Legal limitations placed on the personnel involved in patient care preclude utilization of on-the-job training as a substitute for formal education and experience.

To this end, the officers and councilors of the California Medical Association remind all licensed

practitioners of medicine in the State of California to be alert to legal limitations imposed on them and other personnel in the health care field. All members of the "health team" should be utilized to their fullest capacity but they should not be asked to extend themselves beyond the limits of their qualifications, license or certification.

Approved by the CMA Council 26 August 1967.

Constitutional Amendments

FOR ACTION IN 1968

One constitutional amendment was introduced in the 1967 House of Delegates and, under the terms of the Constitution, must lie on the table until the next regular meeting of the House of Delegates.

This proposed amendment is shown here for the information of the membership. In addition, the proposed Constitutional amendment is required to be printed in two issues of CALIFORNIA MEDICINE before it comes before the House of Delegates for action.

CONSTITUTIONAL AMENDMENT NO. 1-67

Woman's Auxiliary; Article I, Sec. 6

Introduced by: Council

Resolved: That a new Section 6 be added to Article I, as follows:

"Section 6.—Woman's Auxiliary to the California Medical Association.

"In addition to the organizational structure previously set forth in this Article, this Association may charter a Woman's Auxiliary to the California Medical Association, and components there-

to, which shall be considered an integral part of the Association but which shall conduct its own organization and business separate and distinct from the Association and its Societies, subject to the following requirements:

"a. The name of the Auxiliary shall be 'Woman's Auxiliary to the California Medical Association,' (hereinafter referred to as Auxiliary);

"b. The purpose of the Auxiliary shall be to promote the science and art of medicine, the protection of public health and the betterment of the medical profession, and to promote similar interests of its component Auxiliaries;

"c. The Auxiliary shall be composed of the component Auxiliaries and their members;

"d. Component Auxiliaries shall include all women's auxiliaries to component Medical Societies of the California Medical Association heretofore or hereafter chartered by this Association;

"e. Charters to component Auxiliaries shall be granted and revoked by the Association as it may provide; provided that no charter issued by the Association, nor any action of the Association in issuing or revoking such charters, shall conflict with the purposes and principles of this Association as set forth in its Constitution and Bylaws."



❧ In Memoriam ❧

AUSLEN, HARRY, San Francisco. Died 19 May 1967 in San Francisco of coronary arteriosclerosis, aged 72. Graduate of the College of Physicians and Surgeons of San Francisco, 1918. Licensed in California in 1918. Doctor Auslen was a retired member of the Alameda-Contra Costa Medical Association and the California Medical Association, and an associate member of the American Medical Association.



BETTIN, MONA E., Anaheim. Died 24 September 1967 in Anaheim of arteriosclerosis, aged 78. Graduate of Los Angeles Medical Department, University of California, 1912. Licensed in California in 1912. Doctor Bettin was a member of the Los Angeles County Medical Association.



CHAMBERS, FRANCIS REDMOND, Downey. Died 27 August 1967 in Downey of heart disease, aged 55. Graduate of Schools of Surgery, Royal College of Surgeons in Ireland, Dublin, 1943. Licensed in California in 1950. Doctor Chambers was a member of the Los Angeles County Medical Association.



COOKE, WILLIAM C., San Diego. Died 1 October 1967 in San Diego, aged 67. Graduate of Stanford University School of Medicine, Palo Alto-San Francisco, 1926. Licensed in California in 1926. Doctor Cooke was a retired member of the San Diego County Medical Society and the California Medical Association, and an associate member of the American Medical Association.



DOUGLAS, LEE, Van Nuys. Died 12 September 1967 in Palm Springs of heart disease, aged 66. Graduate of the College of Osteopathic Physicians and Surgeons, Los Angeles, 1929. Licensed in California in 1929. M.D. degree from California College of Medicine, 1962. Doctor Douglas was a member of the Los Angeles County Medical Association.



HARK, BERNARD, La Jolla. Died 18 September 1967 in La Jolla of cancer, aged 59. Graduate of Hahnemann Medical College and Hospital of Philadelphia, Pennsylvania, 1932. Licensed in California in 1946. Doctor Hark was a member of the San Diego County Medical Society.



HEALD, ELIZABETH SCHULZE, Berkeley. Died 30 September 1967 in Berkeley of carcinoma of the lung, aged

71. Graduate of the University of California School of Medicine, Berkeley-San Francisco, 1917. Licensed in California in 1917. Doctor Heald was a member of the Alameda-Contra Costa Medical Association.



HIRSCHBERG, EDWARD MORTON, Salinas. Died 24 August 1967 in Salinas, aged 54. Graduate of the University of Colorado School of Medicine, Denver, 1936. Licensed in California in 1938. Doctor Hirschberg was an associate member of the Monterey County Medical Society.



JACKSON, ERNEST ROBERT, Berkeley. Died 26 September 1967 in Berkeley of heart disease, aged 68. Graduate of the University of California School of Medicine, Berkeley-San Francisco, 1929. Licensed in California in 1929. Doctor Jackson was a retired member of the Alameda-Contra Costa Medical Association and the California Medical Association, and an associate member of the American Medical Association.



LEES, JAMES KIMBER, Torrance. Died 19 September 1967 in San Pedro, aged 45. Graduate of Tulane University School of Medicine, New Orleans, Louisiana, 1946. Licensed in California in 1947. Doctor Lees was a member of the Los Angeles County Medical Association.



MCGREGOR, HELEN, Long Beach. Died 7 July 1967 in Lynwood of metastatic carcinoid tumor, aged 62. Graduate of the University of Southern California School of Medicine, 1938. Licensed in California in 1938. Doctor McGregor was a member of the Los Angeles County Medical Association.



PEGO, RICARDO A., Pacoima. Died 10 September 1967 in Granada Hills of cancer of brain, aged 47. Graduate of Universidad de la Habana Facultad de Medicina y Farmacia, Cuba, 1946. Licensed in California in 1954. Dr. Pego was a member of the Los Angeles County Medical Association.



TEMPLETON, HARRY JOHN, Carmel. Died 26 September 1967 in Carmel Highlands, aged 72. Graduate of The Ohio State University College of Medicine, Columbus, 1917. Licensed in California in 1925. Doctor Templeton was a retired member of the Alameda-Contra Costa Medical Association and the California Medical Association, and an associate member of the American Medical Association.

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1968 ANNUAL SCIENTIFIC ASSEMBLY

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Director
Office of Comprehensive Health Planning
Office of the Surgeon General
United States Public Health Service

TOD H. MIKURIYA, M.D.

Commissioner
Food and Drug Administration

CHARLES A. CHIDSEY, III, M.D.

Associate Professor of Medicine
Head, Section on Clinical Pharmacology
University of Colorado School of Medicine

CECIL HOUGIE, M.D.

Associate Professor of Pathology
University of Washington School of Medicine

DANIEL DEYKIN, M.D.

Assistant Professor of Medicine
Harvard Medical School

TOD H. MIKURIYA, M.D.

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House of Delegates Opening Session, Mark Hopkins, Saturday evening, March 23;
 Scientific Sessions, Fairmont Hotel, begin Sunday morning, March 24.

1. Fill in the form below **completely** for room accommodations at the CMA's 1968 Annual Session. There is only a limited number of rooms available. Your choice of accommodations will be better if your request is for rooms to be occupied by two or more persons.
2. Your reservation request should include the definite date and hour of your arrival and departure.
3. All reservations must be made through the CMA Housing Bureau, Fox Plaza—Suite 260, San Francisco, California 94102 by *March 1, 1968*.

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| SIR FRANCIS DRAKE Powell and Sutter | 15-22 | 19-26 | 70 |
| HANDLERY INN 260 O'Farrell | 20-26 | 24-30 | None |
| CHANCELLOR HOTEL 433 Powell | None | 13-15 | None |
| PLAZA HOTEL Post and Stockton | None | 14-17 | None |

*Rates subject to change

Send to: CALIFORNIA MEDICAL ASSOCIATION—*Housing Bureau*
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Please reserve the following accommodations for the CMA's 1968 Annual Session in San Francisco, March 23-27. House of Delegates Opening Session, Saturday, March 23, at the Mark Hopkins; Scientific Programs begin Sunday morning, March 24, at the Fairmont.

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—PLEASE PRINT OR TYPE—

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WOMAN'S AUXILIARY

to the California Medical Association

Courier

DURING THE PAST YEAR, there have been several innovations in the format of *Courier*, all of which we hope have resulted in an improved Auxiliary publication for your wives.

At the annual meeting in April 1967 in Los Angeles, a questionnaire was submitted to the body of delegates. It gave the editors ideas and suggestions as to what the members would like to see in *Courier*. Many of these have been or soon will be incorporated in future issues. A controversial question was whether the membership would agree to the sale of advertising space in *Courier* if that could be done through the advertising office of the CMA, and whether they would approve the selling of *Courier's* mailing list to advertisers. All this with a thought of obtaining funds to buy articles from professional authors, color illustrations, etc. About 140 questionnaires were received back. The response was as expected—three-to-one in favor of advertising, but two-to-one against the selling of the list. At this date, the entire idea has been dropped.

From the available budget, the services of a talented young commercial art student, Mr. David Alcorn, were obtained. Four new covers have been designed by Mr. Alcorn, which we feel are a decided improvement. Each design is featured against the background of a medical capsule. The Winter issue is a modern, partridge-in-a-pear-tree with a pair of "pop art" eyes staring at the reader; the Summer issue is a red, white and blue section of the flag; the Fall issue features an autumn leaf and the Spring issue is to be a surprise to the members. In the near future, we hope for another alternate design more traditional in feeling, for the Winter issue.

On the theory that doctors and their families throughout the state are interesting people, three contributing editors were appointed. Their job is to keep abreast of newsworthy items from their parts of the state. In the North, the representative is Mrs. A. E. Warrens of Chico; in the Southland, Mrs. Henry Botzbach of San Marino; in the Middle Valley sections Mrs. Benjamin Packer of Fresno; and the Bay Area will be represented by me and my co-editor, Mrs. Harry Dvorsky of San Leandro, without whom none of this past year would have been possible.

Whether medical families move more than other segments of the population is an unanswered question. But the task of keeping current the mailing files of around 9,500 members was becoming an impossible task for a member of the Auxiliary working in her home. Previous circulation managers have given a great deal of time to keeping up-to-date with the many changes caused by new addresses, the addition of new members, and the weeding out of delinquent members and the files of deceased members. A year ago this job was transferred to the CMA office, where the permanent file has always been and where the *Courier* is mailed. A circulation assistant, Mrs. Edward Tuel-ler of Burlingame, assists in any way she can, usually by obtaining at the Annual Convention and Fall Conference the names of members not receiving *Courier*.

Doctor, once again the plea that you have heard so many times before: Please urge your wife to read *Courier*. We are trying every way, every day, to make it more meaningful and entertaining for her. All the editors welcome your ideas and suggestions, and best of all, tips of where a topical story might be waiting for us.

MRS. HARRY ALTON,
EDITOR, *Courier*

PUBLIC HEALTH REPORT

Lester Breslow, M.D., M.P.H.

Director, State Department of Public Health

DIVORCE AND ITS by-products are an ever-growing problem in California. While some information, such as the annual totals of divorces and annulments had been available for decades, it was not comprehensive enough for legislative or other serious study.

This situation was corrected by the State Legislature when it required that divorce actions be made reportable in more detail beginning 1 January 1966, and added to the vital statistics of births, marriages and deaths.

As early as December 1948 the State Bureau of Vital Statistics, assisted by the county clerks' offices, began compiling the numbers of final divorces and annulments granted by year by county. The yearly compilations provided a Statewide divorce and annulment total, but little more. Legislation at Sacramento established the first statewide registration effective 1 January 1962, and although the resulting centralized registration was an improvement, the meagerness of the data collected still remained a major shortcoming.

The information gathered was less than that required by the Divorce Registration Area of the National Division of Vital Statistics, and California remained excluded from this national data collecting system. The 1966 legislation brings California's reporting into conformity and in 1968 the state will be eligible for admission to the National Divorce Registration Area.

Today the divorce reporting program, administered by the State Bureau of Vital Statistics, is the most comprehensive in the nation in scope of data collected. The growing body of information has significance for physicians, social scientists and attorneys—among other groups—concerned with population growth and the integrity or disintegration of families.

The following data, taken from the first year of comprehensive reporting, may have indirect medical implications.

- Compared with 144,086 marriages during 1966, more than 105,000 initial complaints were filed that same year for divorce, annulment and separate maintenance. How many of them were final is yet to be reported. Of these, nine out of ten cases which began the dissolution process were divorce actions.

- A total of 150,000 children of all ages — 130,000 of them under the age of 18, including 60,000 infants and pre-school children under six years — were members of families in the divorcing population.

- Among divorcing couples with children there was apparently premarital conception in about 25 per cent of the families. Where the wife was under 20 when married, about one-third of those with children apparently had premarital conception.

- Divorcing husbands and wives were younger than married persons in the general population: in median ages the husbands were 34.2 years old and the wives 31 years, when the initial complaint was filed. One-fourth of the couples were married 13 years or longer; for two-thirds of the divorcing persons this had been the only marriage.

The State Bureau of Vital Statistics plans to initiate and encourage special studies based on data from the reporting program. The variety and quantity of data on divorce that is now being collected should enable qualified investigators to expand knowledge in the field of family dynamics.

The statute establishing the current reporting program runs until 31 December 1969. This will provide an opportunity, in the latter part of 1968, for a thorough review of the utilization of the data made available through this reporting program. By then the accumulated data and findings should provide the legislature with sufficient basis to determine whether the reporting program is to be terminated, or modified and continued.

INFORMATION

Self Medication Practices

A Report of the Bureau of Research and Planning,
California Medical Association

A recently published study observes that lay people control not only decision-making about the health professionals they consult and whether or not they accept the advice they receive, but also about their own care, i.e., self-medication. The authors state that self-medication, which they and others term "folk medicine" is increasing in prominence in relation to its counterpart, professional medicine.

Reasons for this shift include, among others, changing disease patterns, shortages of health personnel, and greater public interest in and knowledge about matters of health.

The study also stated that the average household had almost 30 different medications on hand, only five of which were likely to be prescriptions. Two-thirds of all purchases of medications were self-determined. There was, as expected, considerable variation in who motivates such purchases according to types of illness involved. If the feasibility study serves no other purpose, its primary value lies in suggesting the areas in which health education and information may be required.

Introduction

A feasibility study* to secure information on the self-medication practices of the public was recently conducted in households in a San Francisco Bay Area community. In addition to socio-economic data concerning the households included, the investigators obtained information concerning medications on hand in the house and medications purchased during a two-week period. Although there were slight variations in socio-economic characteristics between households surveyed and all households in the census tracts, data are reported

to be representative of general patterns.

The authors indicated in their introduction that there has been a shifting in the boundary between professional and folk medicine in recent years. There are several reasons for this shift: (1) changes in disease problems, (2) shortages in many of the health occupations, (3) growing public knowledge about and interest in health matters, (4) changes in methods of financing medical care, and (5) greater government control over enterprises affecting the health of the public.

Because of the growing importance of self-medication, the authors sought to determine purchasing and usage patterns of drugs, whether or not they were prescribed, who suggested them, whether there is significant correlation between patterns and education of family members, and what types of illnesses are most frequently self treated.

Use of Medications Analyzed

The most frequent use of medications on hand was for skin problems, followed by respiratory and gastrointestinal ailments. Medications purchased were most often used for respiratory, central nervous system, gastrointestinal, and general systemic problems, respectively. Considerably more than one-third of all medications were for the entire family, and less than one-third were obtained for the use of specific individuals (mainly the wife).

As shown in Table 1, the 86 responding households had 2,539 medications on hand that were used for 2,623 purposes. The number of medications per household ranged from three to 88, with an average of 29.5. Many individuals had medications on hand that were for their children who are now adults living in their own homes. One respondent inherited her mother's estate, including the medications. Medications are often moved with the family furniture when a household is relocated in another geographic area. Of the total medications on hand, 445 were prescriptions and, of these, only 346 carried labels identifying the medication.

Reasons Given for Drug Purchases

Two-thirds of the decisions to purchase the medications on hand were self-determined, while more than one-fourth were advised by physicians and members of the health professions other than pharmacists. The participants accepted professional advice on medications for cardiovascular and genitourinary problems in most instances. For sys-

*Roney, James G., Jr., and Nall, M.L.: Medication Practices in A Community: An Exploratory Study; Stanford Research Institute, Menlo Park, August 1966.

Reprint requests to: 693 Sutter Street, San Francisco 94102.

temic and CNS problems, acceptance was about one-half to one-third, respectively. For all other categories, medications were self-determined in two-thirds or more of the cases. Other sources of advice in all categories were negligible.

Although the medications on hand differed with the educational level of the head of the household, the study did not attempt to probe into these relationships. The authors suggest, however, that this may be related to the educational level, or to such factors as age, family composition, or sociocultural factors.

Purchases Made During Survey Period

Besides indicating what medications they had on hand participants were required to record those purchased during a two-week period. During this

time 61 of the 86 households bought medications. Many of those who did not said that this was not unusual, since no family member had been ill during the period. Chronic conditions, on the other hand, were often associated with purchases in large quantities among families studied.

A total of 154 medications were acquired by the 61 households, of which 40 were prescription items, 94 were over-the-counter drugs and 20 were from other sources (samples, dispensed at work, etc.). All prescriptions written during the period were filled.

In addition to those purchased or received as samples, respondents were asked about other sources of medications. Only seven indicated that they received medications from neighbors or relatives. In general, the respondents felt that it was not a good practice to borrow other people's medicines.

Usage of Homemade Remedies

Nine households prepared homemade remedies during the two-week period. The remedies included mixtures of honey, lemon, and hot water for colds and coughs; gelatin and water to prevent menorrhagia; and witch hazel and salt or boiled California oak bark for poison oak dermatitis. Many respondents stated that in the past they had prepared homemade remedies for boils, gum sores, and upper respiratory infections. Others recalled tonics made by their parents and grandparents, as well as remedies for rashes, swollen ankles, and other ailments. There was some evidence that the homemade remedies of the past have been replaced by over-the-counter preparations.

Sources of Advice About Drugs

The sample was asked who had advised them concerning the medications obtained during the period. Sources of advice for all types of medications, regardless of their purpose, are shown in Table 2.

| TABLE 1.—Uses of Medications on Hand | | |
|--------------------------------------|-----|--------|
| Category of Use | | Number |
| Systemic | | 273 |
| Nutritional supplement | 110 | |
| Metabolic disorder | 46 | |
| Fever | 23 | |
| Allergy | 80 | |
| Other | 14 | |
| Central nervous system | | 275 |
| Nervousness | 32 | |
| Pain | 58 | |
| Headache | 137 | |
| Other | 48 | |
| Eyes | | 69 |
| Eye irritation | 58 | |
| Other | 11 | |
| Respiratory system | | 565 |
| Upper respiratory infection | 374 | |
| Ear | 28 | |
| Cough | 120 | |
| Other infection | 43 | |
| Cardiovascular system | | 33 |
| Gastrointestinal system | | 341 |
| Indigestion | 133 | |
| Diarrhea | 35 | |
| Constipation | 76 | |
| Hemorrhoids | 40 | |
| Other | 57 | |
| Genitourinary system | | 66 |
| Musculoskeletal system | | 92 |
| Muscle pain | 78 | |
| Other | 14 | |
| Skin | | 725 |
| Poison oak | 50 | |
| Cuts | 221 | |
| Irritation | 135 | |
| Insect bites | 25 | |
| Burns | 69 | |
| Sunburn | 65 | |
| Canker sore | 33 | |
| Fungous infection | 61 | |
| Other | 66 | |
| Other | | 184 |
| Lubrication | 29 | |
| Antiseptic | 25 | |
| Rubbing | 42 | |
| Bathing | 27 | |
| Not stated | 61 | |
| Total | | 2,623 |

| TABLE 2.—Sources of Advice for All Medications Acquired During a Two-Week Period | | |
|----------------------------------------------------------------------------------|--------|----------|
| Source | Number | Per Cent |
| Self | 82 | 53 |
| Physician | 60 | 39 |
| Pharmacist | 4 | 3 |
| Dentist | 2 | 1 |
| Other | 6 | 4 |
| Total | 154 | 100 |

Differences According to Condition

When specific disease conditions are examined

for source of advice, distinct differences were indicated. As shown in Table 3, within the respiratory group, upper respiratory infections and coughs tended to be treated by self-medication, while ear problems were treated with professionally advised medications. Other infections were about evenly divided between the two.

Sources of advice for the gastrointestinal group also showed variations, as seen in Table 4. Self-advised medications were used primarily for indigestion and constipation. Medications for hemorrhoids followed a similar pattern, but showed increased representation among the pharmacists. Diarrhea preparations were about evenly divided between self-advice and professional advice, but other gastrointestinal preparations, including ulcer and gall bladder medications, were predominantly advised by the health professions.

Health Information Media Indicated

The sources of medical information used by the households included magazines and newspapers,

TABLE 3.—*Sources of Advice as to Use of Drugs—Respiratory Category*

| Condition | Self | Health Profession | Friend | Pharmacist | Relative | Other |
|-------------------|------|-------------------|--------|------------|----------|-------|
| Upper respiratory | | | | | | |
| Infection . . . | 78.1 | 14.4 | 1.9 | 0.3 | 1.3 | 4.0 |
| Ear | 7.1 | 89.3 | | 3.6 | | |
| Cough | 61.7 | 24.2 | | 0.8 | 2.5 | 10.8 |
| Other infection | 46.5 | 44.2 | | 2.3 | 2.3 | 2.3 |

TABLE 4.—*Sources of Advice as to Use of Drugs—Gastrointestinal Category*

| Condition | Self | Health Profession | Friend | Pharmacist | Relative | Other |
|-------------------|------|-------------------|--------|------------|----------|-------|
| Indigestion . . . | 82.0 | 15.0 | 1.5 | | 1.5 | |
| Diarrhea | 51.4 | 45.7 | 2.9 | | | |
| Constipation . . | 78.9 | 14.7 | 1.3 | | 1.3 | 2.6 |
| Hemorrhoids . . . | 70.0 | 17.5 | | 7.5 | 2.5 | 2.5 |
| Other | 17.5 | 77.2 | 1.8 | 1.8 | 1.8 | |

books, consumer reports, and television. Although most of the respondents watched television, the majority denied that it influenced their medication practices. About three-fourths looked to magazines and newspapers for current information. Many indicated that they referred to these sources to obtain information on specific subjects, such as birth control. Almost half of the sample read books dealing with health and medical topics. A little less than one-third consulted consumer reports. In general the sources of information varied with the category of medication, with specific problems in those categories, and with the educational level of the participant.

Conclusions

The authors conclude that, although this study demonstrated the feasibility of conducting community surveys to delineate the folk-professional boundary in medication practices, additional community studies are needed, since these findings are based on a small sample and the respondents consisted of only those people who chose to cooperate. While the sample was not totally representative of the two census tracts surveyed, the results do shed some light on the subject. Further research is needed, they state, on self-medication practices, on the level of medical knowledge of lay persons, and on other factors affecting decisions concerning medication and treatment.

"The changing relationship between the health professions and the laity," they say, "will have impacts on health and medical education, public education, legislation that limits medication purchases, policies on the financing of medical care, and, in industry, production and market planning for products that affect public health."



NEWS & NOTES

NATIONAL • STATE • COUNTY

LOS ANGELES

Dr. Elmer R. Jennings of Long Beach received the 1967 John Elliott Memorial Award of the American Association of Blood Banks at the annual meeting of the organization held recently in New York. The award, a scroll and \$500, is presented in memory of the late Dr. John Elliott of Miami, a pioneer in blood banking.

It was given to Dr. Jennings for "improvement of blood banking standards" and "for his many contributions to the association."

* * *

Dr. James V. Dooley has been appointed director of programs, continuing education, in the Postgraduate Division of the USC School of Medicine. In his new assignment Dr. Dooley will plan and coordinate continuing education courses of interest to practicing physicians and hospital professional personnel.

SAN FRANCISCO

The Dr. J. Elliot Royer Award for 1967 has been given to Dr. Alfred Auerback, an associate clinical professor of psychiatry at the University of California San Francisco Medical Center. Presentation of the award and a check for \$10,000 to Dr. Auerback was made by Dr. Stuart C. Cullen, dean of the School of Medicine, on behalf of the Regents of the University of California.

The award was established under the terms of the will of the late Dr. Royer. It was his wish that each year a medical person in the San Francisco Bay area be recognized for the most significant contribution to the advancement of psychiatry and neurology. The award was given to Dr. Auerback for his contributions to community psychiatry.

Dr. John J. Sampson was presented with the Gold Heart award of the American Heart Association at the recent annual meeting of the organization in San Francisco. The award was given in recognition of significant volunteer contributions to campaigns against heart disease.

SANTA CLARA

A new experimental training program in investigative medicine will be initiated by the Stanford University School of Medicine. The program will be funded by a \$143,000 grant from the National Institutes of Health. Dr. Halstead R. Holman, Guggenhime professor and executive head of the Department of Medicine, will direct the program for medical students and postdoctoral fellows. He will be assisted by Dr. Thomas Merigan, associate professor of medicine and head of the Division of Infectious Diseases, and Dr. Hugh McDevitt, assistant professor of medicine.

"Investigative medicine increasingly requires a proficiency of clinical analysis and management of individual patients and a detailed, imaginative use of experimental biological techniques in studying problems presented by the patient," Dr. Holman said. "It is our hope that the new program will meet this requirement — training physicians for careers in academic internal medicine and enabling them to function as investigators, teachers, and clinical specialists."

GENERAL

Dr. Lester Breslow, director of the California State Department of Public Health, was named president-elect of the American Public Health Association at the annual meeting of the association in Miami in October.

* * *

The Arizona regional scientific meeting of the American College of Physicians will be held 9 December at the Skyline Country Club, Tucson, Arizona. Further information may be obtained from Hayes W. Caldwell, M.D., 555 West Thomas Road, Suite 134C, Phoenix, Arizona 72205.



The Physician's BOOKSHELF

CALIFORNIA MEDICINE does not review all books sent to it by the publishers. A list of new books received is carried on page 56 of the Advertising Section.

MANUAL OF PREOPERATIVE AND POSTOPERATIVE CARE—Committee on Pre- and Postoperative Care, American College of Surgeons—Editorial Subcommittee: Henry T. Randall, M.D., Chairman, James D. Hardy, M.D., and Francis D. Moore, M.D. W. B. Saunders Company, West Washington Square, Philadelphia, Pa. (19105), 1967. 506 pages, \$8.50.

This publication is a highly readable and compact manual addressing the problems of preoperative and postoperative care of the surgical patient on both a theoretical and practical basis. The individual sections are written by surgeons of considerable proficiency and stature in their fields. Their contributions have been nicely edited and integrated by the Committee on Pre- and Postoperative Care of the American College of Surgeons.

The format is divided into two sections: general principles and the management of problems associated with the various organ systems. In most areas, sufficient detail is incorporated into the text, while treatment in other areas is somewhat superficial and elementary. In general, however, the coverage is appropriate in breadth and depth. Particularly outstanding are the sections on fluid and electrolyte therapy, metabolic response to injury and the cardiovascular system in the care of the surgical patient.

I highly recommend this manual as both a quick and complete review for the busy surgeon and as a reference work for physicians in training. I would recommend it even more vigorously to medical specialists who deal with patients in the postsurgical period.

DANIEL S. THEARLE, M.D.

* * *

HANDBOOK OF ORTHOPAEDIC SURGERY—Seventh Edition—Alfred R. Shands, Jr., B.A., M.D., F.A.C.S., Medical Director of the Alfred I. duPont Institute of the Nemours Foundation; Visiting Professor of Orthopaedic Surgery (Emeritus), University of Pennsylvania School of Medicine, Philadelphia; R. Beverly Raney, Sr., B.A., M.D., F.A.C.S., Professor of Orthopaedic Surgery and Chairman of Division of Orthopaedic Surgery, University of North Carolina School of Medicine; with the collaboration of H. Robert Brashear, B.A., M.D., F.A.C.S., Associate Professor of Orthopaedic Surgery, University of North Carolina School of Medicine, Chapel Hill. The C. V. Mosby Company, 3207 Washington Blvd., St. Louis, Mo. (63103), 1967. 572 pages, 269 illustrations, 85 pages of bibliography, \$12.00.

In this 7th edition, more comprehensive coverage has been skillfully achieved. Whereas the earlier editions were principally for non-orthopedic physicians, medical students, and paramedical groups, the present edition, while it has the same appeal in non-orthopedic disciplines, is well suited for orthopedists.

The authors, distinguished orthopedic surgeons and educators, are eminently qualified for the arduous task of writing an orthopedic textbook. The medical world is indebted to them for their classic, and for astutely keeping it up to date. The fact that the book has spanned 30

years and is now in its 7th edition is testimony to its usefulness and popularity.

As would be anticipated, additional space has been allocated to those entities and techniques which have moved up in clinical importance, and less coverage given entities such as poliomyelitis, which fortunately, have moved far down the clinical ladder.

In the first 15 chapters, related entities are grouped together; the last seven chapters present entities as they involve specific skeletal system articulations and regions.

The 269 illustrations, uniformly of high quality, include numerous radiograms reproduced in the positive. Because no textbook with broad coverage can present sufficient information to satisfy the earnest student, the authors have appropriately included 85 pages of bibliography updated to 1967.

The publisher deserves commendation for the exceptionally fine physical qualities he has given to this time-tested book.

As in all of the scientific disciplines, the area of knowledge in orthopedic surgery is increasing at a phenomenal rate. This places heavy responsibility on authors of textbooks. Doctors Shands and Raney and their collaborator, Doctor Brashear, have ably met this challenge.

J. VERNON LUCK, M.D.

* * *

COCCIDIOIDOMYCOSIS—Papers from the Second Symposium on Coccidioidomycosis—Edited by Libero Ajello, National Communicable Disease Center, U.S. Dept. of Health, Education and Welfare, Atlanta. Publication Arrangements Under the Direction of the Arizona State Department of Health. The University of Arizona Press, P.O. Box 3398, College Station, Tucson, Arizona (85700), 1967. 434 pages, \$15.00.

Before reviewing the proceedings of this Second Symposium on Coccidioidomycosis, which was held in Phoenix, Arizona, on 8 to 10 December 1965, one must recall the First Symposium which was also held in Phoenix on 11 to 13 February 1957. The collection of papers that comprised the proceedings of this First Symposium numbered 31, and 250 persons were in attendance. Since then the proceedings of the First Symposium have become a collector's item; the number of copies printed being far short of the final demand.

The number of papers presented at the Second Symposium totaled 63, and a comparison of the two groups of presentations is indicative of the advance in knowledge of coccidioidomycosis, particularly in treatment, that has occurred during the interval between 1957 and 1965.

The Second Symposium has an international aspect with the attendance of 63 persons from outside of the United States, including representatives of South America, Central America and England. The total registration for the Second Symposium reached a total of 458. The international speakers emphasized the existence of coc-

coccidioidomycosis and extension of the endemic areas into Central America and Mexico, in addition to Argentina and Venezuela. Isolated cases were also described where infection was transmitted via packing material that arrived, for example, in Britain, and that had been contaminated by *C. immitis*. In the report by the British author, Dr. William Symmers, coccidioidomycosis is seen in Britain, not only because people travel, but also because the disease itself may travel in such materials originating from within the endemic area of the United States.

In the Second Symposium, one learns that definite advances have been made in the treatment of coccidioidomycosis with the development and use of amphotericin B. Although amphotericin B must be given intravenously for the control of disseminating coccidioidomycosis, its toxic effects remain important, but appear to be dose related. Of these, nephrotoxicity is most important and regulation of dosage, ordinarily not to exceed a total of 5 gm, will be tolerated. The intrathecal administration of amphotericin B is necessary for the control of coccidioid meningitis and particularly via the cisterna magna. The introduction of the Ommaya ventricular catheter and reservoir is to be considered when the infection has reached the level of the ventricular space and also when intracisternal injections cannot be carried out. Surgical aspects of the disease process have also been given more consideration. These include not only the thoracic approach for pulmonary lesions (pulmonary cavities and abscesses), but also the orthopedic treatment of destructive bone lesions and neurosurgical therapy, particularly when obstruction of the cerebrospinal fluid circulation has occurred due to coccidioid meningitis.

Of recent interest is the production of *Coccidioides immitis* vaccine, made from the spherule wall of the organism, and with which the first human trials are now under way.

In diagnosis, new tests have been introduced such as the immunodiffusion test as a substitute for complement fixation, and the agar-gel precipitin-inhibition tests. These seem useful more from the screening standpoint, rather than for guidance of treatment and do not replace the quantitative complement fixation tests so well developed by the late Charles E. Smith.

It was indeed fortunate that during the Symposium a banquet was held in honor of Dr. Charles E. Smith, which provided an opportunity for this distinguished investigator to outline in detail his personal experiences with coccidioidomycosis. The early phases and tales of the work of this dedicated investigator of the disease are most interesting and have now become a permanent record and will undoubtedly make the Proceedings of the Second Symposium on Coccidioidomycosis also a collector's item. The volume has been fittingly dedicated to Dr. Smith who died in April of 1967.

The papers comprising the Second Symposium on Coccidioidomycosis portray the wide extent of the disease and its importance as a public health problem in this country. The considerable interest in its manifestations and the challenges of present day therapy are reflected in the numbers of investigators that continue to be intrigued by the various pathologic manifestations produced by the fungus, *C. immitis*.

Dr. Libero Ajello, the editor, is to be complimented on the preparation and appearance of the volume which is available in both hard and paper covers. The former is preferable in the medical library where the volume will be frequently referred to as a useful reference in present day aspects of coccidioid disease, including its diagnosis and treatment.

WILLIAM A. WINN, M.D.

COMPLICATIONS IN SURGERY AND THEIR MANAGEMENT—Second Edition, with contributions by 52 authorities—Edited by Curtis P. Artz, M.D., F.A.C.S., Professor of Surgery and Chairman of the Department, Medical College of South Carolina; and James D. Hardy, M.D., F.A.C.S., Professor of Surgery and Chairman of the Department, University of Mississippi School of Medicine. W. B. Saunders Company, West Washington Square, Philadelphia, Pa. (19105), 1967. 888 pages, \$24.00.

The aim expressed by the editors in the first edition of this book (1961) was "to warn against complications, . . . to suggest methods of prevention, and to provide the best available knowledge about therapy." The present volume, although it is about 200 pages shorter, is more comprehensive in coverage. It is intended as a reference book.

The emphasis is on prevention and the discussions of preoperative management and operative technique are excellent. The first third of the book is devoted to general information. The remainder deals with the problem of specific organ systems.

The editors have assembled a notable roster of authors and have retained over two-thirds of the original group. In general, these men have made few changes. Several chapters were eliminated such as those on diabetes, surgery of the lymphatic system and of the aged. Others were consolidated into other chapters such as pain, antibiotics and venous surgery. New illustrations have been added as well as sections on cancer chemotherapy, closed cardiac compression, and vagotomy and pyloroplasty. The chapter by Noer on wound complications is an excellent, thorough review. Shires' section on fluid therapy is clear and concise.

The major problem of this book is one that is common to any merger of many authors and that is repetition. Many of the changes in this present edition have served to diminish this problem.

The authors have created an excellent reference book which should be indispensable to the surgical resident and a valuable guide to surgeons in general.

ROBERT S. OZERAN, M.D.

* * *

ATLAS OF INTESTINAL STOMAS—Rupert B. Turnbull, Jr., M.D., F.A.C.S., Head, Department of Colon and Rectal Surgery, The Cleveland Clinic Foundation, Cleveland, Ohio; and Frank L. Weakley, M.D., Department of Colon and Rectal Surgery, The Cleveland Clinic Foundation, Cleveland, Ohio. The C. V. Mosby Company, 3207 Washington Boulevard, St. Louis, Mo. (63103), 1967. 207 pages, \$21.50.

The authors and publisher have produced an excellent atlas of techniques for the construction and revision of ileostomies and colostomies. It illustrates and discusses techniques to be used in a variety of clinical situations.

Ileostomy and colostomy procedures are described in separate sections each of which is introduced by a pertinent historical review. Using drawings based upon photographs taken in the operating room each step of the various procedures is clearly depicted. Succinct descriptive legends accompany the illustrations and provide a clear commentary on the techniques.

The most valuable aspect of the atlas is its presentation of techniques to be used in extraordinary situations. These include construction of loop ileostomy and its conversion to end ileostomy, ileostomy in obesity, ileostomy prolapse, ileostomy transplantation and procedures for the correction of stricture. Many refinements in the techniques of colostomy are presented. Particular emphasis is placed upon suture of the colon wall to skin and subcutaneous tissues to provide a well healed mucocutaneous junction and prevent stricture formation.

The only criticism of the atlas one could offer is its failure to discuss the immediate postoperative care of ileostomies and colostomies. The various appliances, tech-

niques of application and regimens for local skin care should have been presented.

This atlas is the most complete work available on the construction and revision of enterostomies. It is based on the extensive experience of its authors and it will serve as a useful guide for both the resident and the graduate surgeon.

ARTHUR L. GOLDING, M.D.

* * *

CIBA FOUNDATION COLLOQUIA ON ENDOCRINOLOGY, Volume 16—Endocrinology of the Testis—Edited by G. E. W. Wolstenholme, O.B.E., M.A., F.R.C.P., F.I. Biol., and Maeve O'Connor, Little, Brown and Company, 34 Beacon St., Boston, Mass. (02106), 1967. 331 pages, \$12.50.

This is the sixteenth and final volume in the series of international Colloquia on Endocrinology. With Dr. R. I. Dorfman of the Institute of Human Biology, Palo Alto, California, as chairman, twenty-six international authorities present and discuss the results of recent research dealing with the endocrinology of the testis.

Much of the material is somewhat esoteric for the practicing physician, dealing as it does with such matters as cytochemistry, steroid biosynthesis, and the testicular enzymes. On the other hand, it will be fascinating reading and important information to anyone interested in such phases of testicular function.

Many cryptic facts of interest to the clinician also can be picked from the well-edited discussions of the hormonal development and relationship of the testis and other generative organs, such as the fact that complete spermatogenesis and fertility are possible in the absence of Leydig Cells; that excellent sperm counts can be obtained in patients with infantile testes by the injection of human menopausal gonadotropins; that plasma testosterone levels are not significantly different in young and old men, probably due partly to falling metabolic clearance rates; that over two-thirds of the estrogen produced in men comes from the testes; and, that human chorionic gonadotropin and ACTH will retard the degeneration of an ischemic testis.

A new syndrome of primitive testicular hypogonadism of probable genetic etiology, called "mixed testicular dysgenesis," is described and will interest the practitioner.

EARL F. NATION, M.D.

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CLINICAL OBSTETRICS AND GYNECOLOGY—Volume 10, Number 2, June 1967—Trophoblastic Disease—Edited by Donald P. Goldstein, M.D., and Hazel Gore, M.B., B.S.; and Ovulation, Edited by Luigi Mastroianni, Jr., M.D. Published quarterly by Hoeber Medical Division, Harper & Row, Publishers, 49 East 33rd Street, New York, N.Y. (10016), about 1,200 pages per year. Subscription: \$18.00 per year.

This volume of Clinical Obstetrics and Gynecology presents symposia on trophoblastic diseases and ovulation. While the need for ovulation induction and the occurrence of trophoblastic disease are relatively infrequent in the experience of the specialist, they nevertheless occupy a position of particular interest in current obstetrical and gynecological thought. The articles of both symposia present the views of eminently qualified investigators and clinicians who have devoted their experience to each of these subjects.

The symposium on trophoblastic disease rightfully is dedicated to Doctors Arthur T. Hertig and Roy Hertz who have inspired investigation and elucidation in the field of the normal trophoblast and its tumors. This symposium consists of selected papers presented at the first New England Workshop on trophoblastic tumors held in

Boston, Massachusetts in February of 1966. The review is a dynamic and enlightening one reflecting the first ten years of experience in the era of chemotherapeutic management of trophoblastic disease. Primary emphasis is placed upon the diagnosis and management of these tumors. Clinicians will take especial interest in Dr. Lewis' paper which outlines time and dose regimens for the use of methotrexate, actinomycin D and chlorambucil. The safeguards in the use of these agents are carefully discussed. Doctors Goldstein and Reid in presenting the problems of molar pregnancy have brought to our attention a relatively new concept in the management of hydatidiform mole. They supply encouraging data to suggest the efficacy of prophylactic chemotherapy prior to the delivery of a molar gestation. Results of therapy imply a considerably decreased incidence of subsequent chorioadenoma destruens and choriocarcinoma. Other sections of this symposium deal with the important and sophisticated techniques of human chorionic gonadotropin assay and their utilization in the detection of and follow up of molar disease. The pathologist is rewarded in reviewing this symposium by reading the authoritative views of Doctors Gore and Hertig, who have devoted themselves to the histologic interpretation of trophoblastic disease. This section brings into sharp focus the importance of the differential diagnosis and the pitfalls encountered in the histologic delineation of these tumors.

Trophoblastic Disease is a short group of articles that succinctly portrays the current status of our knowledge regarding trophoblastic tumors. The articles are well written and while devoted only in part to the requirements of the clinician, effectively and definitively define the diagnosis, management and outcome of trophoblastic disease. Examination of this symposium is essential for every specialist in obstetrics and gynecology.

The section on ovulation is written by a no less impressive group of contributors. Major emphasis is placed on the induction of ovulation. Until recently the treatment of ovulatory failure was one of the major obstacles in the management of infertility. In this volume, the use of recently available clomiphene citrate and human pituitary preparations are presented. Dr. Goldfarb evaluates the current experience with clomiphene in the induction of ovulation. The actions and mode of administration of this drug are assessed. Unfortunately little attention has been given to the number of patients in whom ovulation is induced and more importantly, no notation has been made of the limited number of patients becoming pregnant under a clomiphene regimen. Dr. Gemzell summarizes the experience in Sweden with the use of human pituitary FSH and human chorionic gonadotropin for the induction of ovulation. His experience with these agents is particularly impressive. It is interesting to note that the number of pregnancies and babies produced by this means of ovulation induction is small in comparison with the great attention these drugs have received in the lay press. Other portions of this section on ovulation deal with the anatomy of ovulation, its endocrinology, detection and diagnosis. These reviews express no new information but in encyclopedic form document prior investigation in this area.

These symposia on trophoblastic diseases and ovulation are significant contributions. In this work these subjects which have received wide clinical and investigative interest receive current evaluation. The volume is to be highly recommended particularly to specialists in obstetrics and gynecology.

ROBERT G. GOOD, M.D.



The Radiologist and the Search for Hidden Cancer

The First L. H. Garland Memorial Lecture

LEO G. RIGLER, M.D., *Los Angeles*

I AM DEEPLY HONORED to initiate this series of lectures which we hope will bring to mind from year to year the great services which Dr. Leo Henry Garland rendered to the practice and science of medicine. And I am no less grateful for the chance to pay my respects to the memory of a distinguished physician, one of America's greatest radiologists and one of California's most eminent citizens. But Harry Garland was more than these to me; he was my old and very dear friend; and it is as a friend that I wish to speak of him today. Friendship is not easy to describe; it is not easy to distill liquor on which one has thrived for some thirty-five years into a few brief paragraphs. Harry, with his gift for words could have done it. I can say from personal experience that his deep convictions, his expressiveness, sharp wit and keen judgment tempered by warmth and good cheer made him a magnificent companion.

He liked to test the minds and mettle of his friends. He was as curious about human character as he was about the problems of radiology and explored them both with equal verve. Impatient of fools, impatient of mediocrity, hypocrisy, compromise, Harry Garland shared the difficulties of many brilliant, energetic, principled men.

The facts of Dr. Garland's life are amply cov-

ered in the eloquent biography by Dr. Philip Hodes which appeared in the March 1967 issue of *Radiology*.⁸ Furthermore, in the December 1966 *Bulletin* of the San Francisco Medical Society,¹² Dr. Dwight L. Wilbur has given a word picture of Dr. Garland, the physician and the man. In the hope all of you will read those pieces, I will not review the facts but will instead try, however imperfectly, to recreate for you something of the Harry Garland that we all knew.

Dr. Garland's success as a teacher was due in large measure, I'm sure, to the fact that he never asked more of his students than he asked of himself. If he was impatient of mediocrity, hypocrisy and compromise in others, he would not tolerate them in himself. Devoid of sham, he was courageous in enumerating ideas and equally forthright in voicing protest. Harry Garland was a man of principles, and he had the courage to live by them. When the issues were clear in his mind, when the lines were drawn, there was only one place where Harry could go—to the side dictated by his conscience.

Though deeply religious, Dr. Garland never allowed dogma to check his curiosity or hobble his restless inquiring intellect. He held almost every high office to which a physician could aspire, president of two national societies, trustee of the American Board of Radiology, received the gold medals and all the other honors offered a radiologist in this country. In addition, he was made an

The L. H. Garland Memorial Lecture, presented at the 96th Annual Meeting of the California Medical Association, Los Angeles, April 15 to 19, 1967.

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Honorary Fellow of the Royal College of Surgeons of Ireland and given an honorary degree by his alma mater in Dublin. His research and investigations were of a high order, and his contributions to the literature were not only distinguished but literary as well. He contributed substantially to the advances in radiology these past three decades.

Despite his consuming dedication to the practice of radiology, to the advancement of medicine and particularly to the improvement of medical practice in this state, he nevertheless found the time and energy to be a deeply devoted father and husband. Of course, he was touched by the luck of the Irish in his marriage to Edith Dohrmann, for she shared and matched the depth and variety of his interests. Their home became a gathering place for those who loved the arts and sciences. Together the Garlands promoted some of the finest cultural activities in San Francisco.

Harry Garland was, in the most exacting sense, a true citizen of his country and state. His proudest achievement may possibly have been the development and nurture of the California Radiological Society to which he gave himself unstintingly, sometimes overwhelmingly. The present superior status, economically, professionally, scientifically of radiology in California owes much to his devoted efforts. If at times he seemed to love this work not wisely but too well, that was Harry, that was the way he had to live. He could never give less than all of himself.

Harry Garland was a truly civilized man whose contributions to California recall Emerson's words: "The true test of civilization is not the census, not the crops, no, it is the kind of man the country turns out."

And so Dr. Garland's family is not alone in its loss; we, his friends and colleagues, share it deeply—but not we alone either, for the entire community in which he lived and moved, has been diminished by his death.

Whole men, able to live life intensely and totally, are rare indeed. Harry Garland was one of them, one of that uncommon breed to whom this epitaph, though borrowed, truly applies:

"... the elements so mixed in him that Nature might stand up and say to all the world, This was a man!"

But was his death at the age of 63 necessary? Can we look at this loss and not feel guilty? Guilty that we have not done more about the

problem of cancer, that we have not devoted more of our effort and resources to a disease which has been for so long the cause of pain and sorrow and death.

Where have we failed? For those 65 years of age and over there are 740 deaths per 100,000 population from neoplasms. Compare this with the figure of 46 deaths per 100,000 from accidents. Only cardiovascular diseases cause more deaths than cancer in this age group.

The Rate of Research

We now have mounted a very large and intensive cancer research effort, but it is late, very late. Consider that about 25 years ago the Federal Government was spending only \$3,000,000 on all medical research, the individual states almost nothing, the private foundations a very small amount.

But research is proceeding—at a rate even now perhaps unsatisfactory to most of us, but still progress is being made. The proud boast of the American Cancer Society that we can now cure one-third of all cancer patients as compared with a fourth two decades ago is no doubt correct and is due in part, at least, to the research which has been accomplished. But intensive research, no matter how important, should not deter us from the search, the search for hidden cancer, the cancer which is unknown to the patient, not obvious to the physician. Here lies our opportunity to do something for those who are already afflicted with this disease, and to do it now, without waiting for more spectacular discoveries.

The effort to discover cancers in asymptomatic persons should be undertaken for two reasons: (1) Although there is at present no clear single therapeutic procedure, no cure-all for all cases of cancer, methods are available which are potentially capable of appreciably reducing the mortality if they were widely applied to lesions when small or in an early stage. Likewise, methods are available for detection at an early enough stage to permit salvage of a much greater number of certain cancers than is presently the case.¹ (2) Even if the early detection of small lesions were not to result in any substantial improvement in salvage at the present time, the program should still be pursued. For there always is the possibility that a therapeutic breakthrough may occur at any time. In preparation, we need to gain experience in learning how to discover small cancers in the most effective

and economical way so that if the time comes when a better therapeutic method is available we will be prepared to find the cancers at a time when they are most amenable to therapy—that is, when they are in their earliest possible stage of development.

Internal cancers are difficult to detect. They are present and increasing in size during a considerable period of time while the patient is completely asymptomatic. In some cases, at least, detection during this presymptomatic stage with treatment at that time will lead to far better results. I emphasize detection as distinguished from identification, for if we do not find a lesion, identification will, of course, not be considered.

The search for hidden cancer has been undertaken in a great variety of ways over the years. The problem lies in developing techniques which are both economical of personnel, harmless and effective. Despite extensive investigation, our present methods of detection are relatively crude and not yet highly reliable. Nevertheless, we have enough resources available so that it should be possible for “doctors, not time, to make the diagnosis of cancer.”

In certain situations, the methods for finding hidden tumors are well-known, are reasonably available but are not being used to their fullest extent. The best illustration of this is in carcinoma of the cervix. Therapeutic means are now available which should result in at least 80, possibly 90 per cent salvage of cases of carcinoma of the cervix discovered during the first stage or when in situ.⁴ Means are available, namely, cytological examination, for making a positive diagnosis at a very early stage in almost all cases. But this diagnostic method is not being widely applied; as a result the therapeutic procedure too often must be used in the late stages of cancer of the cervix, not often enough in its earlier stages. The result is a salvage of between 50 and 60 per cent rather than 80 or 90 per cent. This is a failure both in public education and in the education of the medical profession. In part, I believe, it is the result of a reluctance on the part of the medical profession to undertake routine interval examinations of apparently normal individuals. The fact is that only between 15 and 20 per cent of women in the cancer age in the United States are being examined routinely by this method.

As cancer is not a common disease, a very great effort must be expended to find the individual

patient with the hidden lesion in its presymptomatic stage. The very large number of examinations which must be done to find one significant cancerous lesion is illustrated by the data which Gilbertsen⁷ has published from the Cancer Detection Center at the University of Minnesota, where unusually thorough examinations of asymptomatic persons are made. The recent figures indicate that over 13,000 patients had been examined and re-examined at yearly intervals, to a total of more than 64,000 examinations. The total number of cancers found, however, is only 535, and these include a number of skin cancers which no doubt would have been discovered in any case.

Efforts to Improve Methods

Many efforts are being made to improve methods of detection, to make them more feasible, more economical in terms of personnel and less taxing on the part of the patient. You are aware of the many unsuccessful efforts to find a serum or chemical test which would be more sensitive than our present methods of detection, more sensitive even than x-ray examination.

The search for hidden cancer in many sites is now largely a matter of x-ray examination. Identification of the nature of the lesion may require more elaborate diagnostic procedures, but for detection of a lesion of the lungs, the gastrointestinal tract above the sigmoid colon and to a lesser degree the urinary tract, the x-ray examination is the major method. Thus there is a great responsibility thrust upon the radiologist.

There are some immediate rewards even with the relatively crude methods for detection which are available. Gilbertsen⁷ has reported striking improvements in the results of operation in carcinoma of the breast, the rectum and the prostate when the lesion is discovered by routine examination during the asymptomatic period. It is evident that a great deal could be accomplished in carcinoma of the rectum and sigmoid if routine proctosigmoidoscopic examinations were made in all persons in the cancer age at regular intervals. However, no solution has been found for the enormous time factor which is involved in routine proctosigmoidoscopy. It would be patently impossible with our present personnel to examine all those of the cancer age routinely. The superb results which have been reported, however, indicate the desirability of such routine examinations when-

ever it is possible or feasible, particularly amongst persons who present themselves for annual examination. The sad fact is that many such persons who might accept the procedure are not being offered it by their physicians.

The results of therapy of malignant tumors depend to a considerable extent on their stage of development and especially on their size. No doubt there are many small tumors which are already regional or even widespread. There are also large tumors which remain localized. On the whole, however, the smaller the lesion, the better the prognosis; the less the symptoms, the better the outlook. The importance of size is well illustrated by the data recently published by Cutler³ concerning carcinoma of the breast. These data indicate that the size of the lesion in the breast is extremely important as a survival factor.

Even in such malignant tumors as carcinoma of the stomach, size is important as shown by the data published by Comfort and his associates² from the Mayo Clinic. The five-year survival for patients with cancers less than 1.1 mm in diameter was over 80 per cent; for those with lesions less than 2.0 cm, 70 per cent. With increasing size the percentage dropped further. That such small lesions of the stomach can be found by x-ray examination has been repeatedly demonstrated. I would not minimize the difficulties, but there is a reasonable probability of finding lesions in the range of 1 to 4 cm in size and in this group.

From various cancer detection centers the results of operation for cancer of the colon which is still asymptomatic bear out the same contention; namely, that for patients with small tumors or those which are asymptomatic the prognosis is infinitely better than for those commonly seen in practice. That it is possible to detect small cancers in the colon, as small as 1 cm, by x-ray examination has been repeatedly demonstrated. The difficulties, of course, are very great and some lesions of this size or even larger may not be found, but every effort should be made to find them. The combination of proctosigmoidoscopy and x-ray examination of the colon in apparently well persons may well discover a tumor at a time when the outlook is still excellent.

It is, of course, impossible to apply such routine examinations of the gastrointestinal tract and the colon, at least in the present state of our knowledge and of our personnel, to any large segments of the population. But we should continue to examine

selected groups in the hope that we may be able to devise simpler, less expensive, more effective methods.

Asymptomatic Cancer of the Lung

In the lung, especially, the discovery of asymptomatic cancer is of very great importance. The appearance of symptoms in cancer of the lung is usually a poor prognostic sign. And there is little excuse for failing to discover asymptomatic cancer of the lung. For the x-ray examination of the lungs is a relatively simple, relatively cheap procedure which does not require a large amount of personnel time, and, properly done, produces little or no radiation hazard. Once the examination is done, however, the interpretation of the films, the detection of small lesions, must depend on a high index of suspicion, the searching out and analysis of every possible abnormality and a follow-up study to rule out carcinoma. It is possible by routine examination of the chest in apparently well individuals to find lesions in the lung as small as 3 to 5 mm in diameter. As has been pointed out by Garland,⁶ a tumor of this size is already one which is fairly well developed; obviously, our present methods for the detection of tumors are not good enough to determine their presence while still microscopic in size. Nevertheless, the detection of a small lesion even up to 2 cm in diameter, especially when it is in the periphery of the lung, is a signal achievement and should lead to an intensive investigation—if necessary, extirpation with biopsy. At the very least, repeated examinations should be done.

What can be accomplished in such cases? The general pessimism concerning carcinoma of the lung is not entirely justified despite the small series which was reported by Gilbertsen⁷ and the rather larger group reported by Weiss and associates.¹¹ It is clear from the work of Garland and coworkers⁵ and from the studies which we have made that the majority of carcinomas of the lung actually arise as a solitary lesion in the periphery in a segmental or subsegmental bronchus. If seen at this stage, operation can be effective and the prognosis is far better than in the usual large lesions seen in ordinary practice. There are apparently three factors which influence the prognosis. One is the sex of the patient—the outlook is far better in women than in men; the second is the presence or absence of symptoms; and the third is the size of the lesion. Since we cannot change our sex we should at least

try to take advantage of the favorable aspects of the last two criteria.

In connection with this, the data which Cutler³ recently published concerning the survival after operation for carcinoma of the lung are of great importance. Considering only peripheral solitary lesions which are localized, the results are surprisingly good, especially in women. Obviously when the lesion is already regional in its development, the five-year salvage rate drops decidedly.

From California comes an even more striking group of figures gathered by Steele and his associates¹⁰ from the tumor registry indicating, in the case of localized bronchial carcinoma, that in men the five-year salvage following operation is in the range of 35 per cent. In women the figure approaches 70 per cent. It is notable here too, as in Cutler's figures, that not only is the incidence of carcinoma of the lung six or seven times as high in men as in women, but the tumor is far more malignant in men: the mortality rate from lesions of equal size is almost twice as high in men as in women.

Importance of Size in Lung Cancer

The findings of Steele in a large series of peripheral nodules discovered by x-ray examination, all asymptomatic, all operated upon and proved by histologic examination, are highly significant. The latest published data on this study based on a follow-up of practically all the original patients, for five years or more after the surgical procedure, indicate that the survival is only slightly affected by the cell type. But the size is of great importance. The observed five-year survival, without disease, of patients with lesions 2 cm or less in diameter—85 cases—was 53 per cent. In 178 cases in which the lesion was 2.5 to 4 cm in diameter the survival was just under 41 per cent. When the lesion was up to 6 cm in diameter the survival dropped to 29 per cent. The evidence here is clear that size is at least a very large factor. The fact that even in such small asymptomatic lesions, 2 cm or less in size, almost half the patients die within five years indicates the rather malignant nature of the process. Nevertheless, such data contradict the extreme pessimism concerning carcinoma of the lung and give some hope especially because by routine x-ray examination it is not difficult to find lesions in the lungs which are 2 cm in diameter.

How small a lesion can we detect in the lungs and with what degree of certainty can we depend

on x-ray examination for this purpose? Our experience in this regard⁹ is based on the fact that a large number of people are now having x-ray examination of the lungs when they are apparently well. In some of them clinically obvious cancer of the lung eventually develops. A review of the previous films very frequently indicates the presence of evidences of the tumor two to three years before the final diagnosis. In occasional cases the first signs of the lesion can be found from five to ten years before. From the examination of these cases and through studies of many others, we have found many in which the lesion was 1 cm or less in size—and might have been detected—when the patient was first examined. We now have a number of cases in which a lesion less than 1 cm in size was detected on the first examination, was removed shortly thereafter, and the diagnosis confirmed. For example, some time ago I saw a patient with a lesion measuring only 4 mm in size in the roentgenogram. This was removed, microscopic sections immediately done in the operating room and the diagnosis of "oat cell" carcinoma made. Lobectomy was then undertaken and the patient is still alive and well some three years later.

Obviously, the discovery of a small nodule in the lung does not necessarily prove that it is carcinoma. The problem of identification of such small lesions is not an easy one, but it can usually be solved in a variety of ways. Numerous additional x-ray examinations can be made, studies of the sputum, skin tests and so forth can all be done in the hope of determining the nature of the lesion. In many of these cases it will be necessary to do an exploratory thoracotomy and to resect the lesion in order to make a final diagnosis.

While it is true that the results of operation are far better in the isolated peripheral lesion, I should point out that central lesions likewise are amenable to surgical attack if they are found before metastasis has occurred. I have seen long-term survival in a number of such patients whose cancer began in one of the larger bronchi very close to the carina.

The results achieved in small localized lesions should serve to counteract some of the pessimism which prevails in the medical community concerning carcinoma of the lung. Regardless of the final outcome, it is our duty to find these lesions at the earliest possible moment and establish a diagnosis. In order to do this, it is important that

routine roentgenograms of the chest be made frequently, particularly amongst males over the age of 45 who are smokers. Such films should be viewed with a bias toward finding the lesion even though the patient appears to be entirely normal. Too often the fact that there are no symptoms and no physical findings prejudices the physician to the point that he fails to observe or give sufficient credence to a small shadow which may be the first sign of carcinoma. The detection of a lesion at this point may be the difference between life and death for that patient.

Above all it is important that patients with suspicious lesions in the lungs should be closely followed if biopsy or exploratory thoracotomy is not done immediately. Small nodular or infiltrative lesions should not be neglected; reexamination at semiannual intervals should be done to determine whether change in size has occurred. The moment there is some evidence of an increase in the size of the lesion, especially in a person in the cancer age, one must assume that this is a carcinoma and the surgical procedure should be undertaken.

Summary

The search for hidden cancer is neither a hopeless nor an unproductive field, even in the present state of our knowledge of methods of detection and of therapy. Research should be pursued to determine the best methods for the economical and rapid diagnosis of hidden cancer. X-ray examination of the lungs to detect carcinoma should be continued, at least amongst those most vulnerable in the population, in order to gain experience for a future date when more effective therapy will be available. Even now the search for hidden carci-

noma of the lung, gastrointestinal tract, the rectum, colon, cervix and the breast should continue because the available therapeutic results in themselves justify it. In many of these searches the responsibility of the radiologist is paramount. It is he who must find these small lesions and see that they are properly treated. At present it is only by such means that we may reduce the mortality from cancer.

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The Normal Psychological Development Of the American Adolescent

A Review

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■ *Adolescence is a time of life marked by emotional turbulence and turmoil, which creates problems for the adolescent, his family and society in general. The psychological development that occurs during this period can be organized into developmental tasks, which emphasize the purposefulness of adolescence. An awareness of the nine essential tasks of development can serve as a basis for assessing the appropriateness and the developmental level of adolescent behavior. The establishment of a realistic self-concept (identity) is the most basic task of adolescence. Behavioral experimentation, the process through which much of the emotional growth of adolescence occurs, also accounts for the majority of the paradoxical and perplexing actions that typify the adolescent.*

To be in a better position to understand today's teenagers, the physician should not judge normality or abnormality by adult standards, but should view adolescence in reference to its own processes and purposes.

IT IS APPARENT that, during certain eras of history, specific age groups are elevated above the other phases of human life and are given a great deal more thought and attention.¹ Judging by the prodigious amount of literature on the subject, the twentieth century is focused on adolescence—the period of transition from child to adult.

In part, the stimulus for this extra attention

has stemmed from the continued efforts to make sense out of the perplexing and erratic behavior that is characteristic of the adolescent. From an adult's viewpoint, adolescent behavior does at times appear to defy comprehension, and it is this factor which can potentially complicate any dealings with young people of this age group. This is especially true for the physician, who is approached by worried parents and is asked to estimate clinically whether a teen-age patient is acting like a normal adolescent or is showing signs of being emotionally disturbed. Much of the difficulty in the clinical situation seems to be centered in an unsureness or a lack of awareness of what is normal adolescent behavior.

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Presented at the Institute on Adolescent Problems at the Annual Postgraduate Institute sponsored cooperatively by the Sacramento Valley County Medical Societies, Continuing Education in Medicine and Health Sciences, University of California, Los Angeles, School of Medicine, and the Committee on Continuing Medical Education, California Medical Association, Lake Tahoe, June 24 to 26, 1963.

Submitted 9 June 1967.

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The purpose of this paper is to outline and enhance understanding of the normal psychological development that occurs during adolescence by synthesizing data and theories from a variety of sources.

The terms *puberty* and *adolescence* will not be used interchangeably but will be defined more specifically. As used here, *puberty* will refer to the biological and physiological changes associated with sexual maturation. Puberty occurs early in the transition period, taking about two years to be completed and is terminated after all the secondary sexual characteristics have appeared along with reproductive maturity. The term *adolescence* is broader and more inclusive, referring not only to the biological changes but also to psychological maturation and the changes in social status. Adolescence ends when young people complete the transition from childhood by meeting the psychological and socially determined requirements to enter adult life. Thus puberty and adolescence do not necessarily terminate simultaneously; as an example, in Western societies puberty is often completed a number of years before the termination of adolescence.

To avoid getting ensnared in the morass of the cross-cultural differences in adolescence, the sole focus of this paper will be the American adolescent. Before proceeding, it would be appropriate to record some general observations about adolescence as it occurs in our own culture.

- It is a phase in a developmental continuum, which is influenced by what has preceded (childhood) and in turn influences what will follow (adulthood).

- It is a transition period where behavior is characterized by instability, unpredictability and change — a time when actions and emotions are often more extreme, more intense and more unpredictable, and are elicited with less provocation than ever before.

- As compared with that in some other cultures our period of adolescence is more prolonged, usually spanning a ten-year period (approximately ages 11 to 21). Because of this it does not consist of a naturally homogeneous age group and lends itself poorly to generalizations. The factor of prolongation is also responsible for the inherent frustrations caused by having the capacity to function sexually, physically and intellectually as an adult and yet to be told to wait.

- Its onset is usually several years earlier, and

its over-all behavioral effects often less pronounced, in girls than in boys.

- The early phase of adolescence, from approximately 11 to 15, is behaviorally the most difficult and may be developmentally the most critical.^{10,24}

- The process of maturation, both physical and psychological, characteristically proceeds unevenly and asymmetrically.

- Despite the anthropological evidence which validly refutes the popular notion that adolescence is a universal period of turbulence,^{3,19,20} in our society it is marked by storm and stress which creates problems for the adolescent, his family and society in general. In support of this assertion the psychiatric outpatient clinics in this country serve more patients in the 10 to 19 age group than in any other decade of life, that group making up approximately one-fourth of all the clinic patients seen.³⁴ When faced with the bewildering array of adolescent behavior which most often appears purposeless and confusing, it is helpful to view it with a theoretical framework in mind — a theory which, when applied to the behavioral and maturational changes of adolescence, will add organization, understanding and meaning to what is occurring. One of the simplest and most useful theories available for this purpose is the developmental task concept of Robert Havighurst.¹¹ It has the advantage of being flexible and eclectic, and is particularly suited to the task-completion orientation of our society. Briefly, he states that to advance, the individual must master in sequence certain developmental tasks, which are defined by the culture and by individual needs as prerequisites for progressing from one stage of development to the next.

Using this theoretical model as a base to understanding, answers to the following questions will be attempted: What kind of psychological growth takes place during adolescence? What are the developmental tasks and how does the adolescent accomplish them so he can function and be accepted as an adult? Finally, how does this process relate to and explain adolescent behavior?

If adolescence is completed successfully, the over-all result will be psychic growth and individualization. This can be broken down further into nine specific closely related and, at times, overlapping tasks. The tasks, listed below, are not accomplished in sequence, are usually worked on

simultaneously and the time for full mastery may span the entire adolescent period.

1. The establishment of emotional and psychological independence from the parents and other adults.

2. The final arrival at self-definition, which results in the development of a stable self-concept (identity).

3. The development of self-motivation and self-determination.

4. The establishment of an appropriate set of values to be used as a guide for adult behavior and the self-control to implement and adhere to the ethical system selected.

5. The development of empathy and the practice of reciprocity in interpersonal relationships.

6. The establishment of an appropriate sexual identity, which includes the acceptance of oneself as a sexually mature person and leads to the development of meaningful heterosexual relationships.

7. The development of new intellectual capacities and skills.

8. The ability to function satisfactorily with age mates and to behave appropriately in relating to the peer group.

9. The acquisition of training or engagement in a training program that will develop the skills for achieving economic independence.

The establishment of emotional and psychological independence from the parents and other adults. At this time the adolescent begins to question adult (especially parental) authority. He no longer automatically looks up to people in authority, but is more selective, giving respect to those he feels have earned it. He invariably will resist parental influence and opinions. In this process he becomes more skeptical, more argumentative, opinionated and negativistic, and he is notoriously a poor listener. There is much more friction in the family, caused by the conflict between the adolescent's urgent demands for emancipation and the parents' attempts to enforce restrictions. There are arguments over use of the car, dating hours, smoking, drinking, choice of friends, homework, spending money, education and vocational plans and the like. There are insistent demands for privacy; irate indignation can be elicited by opening their mail, by looking into a private drawer, by eavesdropping on telephone calls. Communications between the teenager and parent diminish and there is a distinct pulling away in the direction of

creating and associating in a world apart from parents or other adults.

Arrival at self-definition, which results in the development of a stable self-concept (identity). This is probably one of the most basic tasks of adolescent development, a principle that is acknowledged by many investigators.* Because of its importance and key relationship to the other tasks, it will be explored in more detail. During adolescence the individual develops an accurate, stable and yet expanding set of ideas about what he himself is. The self-concept, or identity, contains both a physical self-image and a psychological self-image. It includes the following: What his capabilities and weaknesses are, ideas about his relationship to society (that is, what he can expect from it and what it can expect from him), ideas about his sexual role, and the formulation of a life plan (what niche both personal and occupationally he will occupy as an adult). What makes the achieving of a unified self-concept so basic and yet so difficult for American youths is that, when faced with becoming adults in our technically advanced, highly complex society, they are presented with a large number of personal choices. The way adolescents generally cope with this potentially confusing situation is to accumulate as much experience as possible and then judge its personal validity by trial and error. Young people cannot be expected to know automatically what kind of person they want to be as adults, without being able to experimentally function in a number of personality and vocational roles. It is pertinent, at this point, to discuss in more detail the important and essential process of experimentation, which is the major method used by the adolescent to accomplish all the developmental tasks. Adolescence is a time for experimentation: time is set aside for youth to experiment with some of the multitude of roles and choices available to them, without criticism or alarm. Appreciation and acceptance of this fact will add immensely to one's understanding of the behavior that typifies the age group.

This experimentation is performed verbally, by actions and in fantasy; and it is partly responsible for the unpredictable and paradoxical nature of adolescent activities.

The experimentation that occurs in fantasy is less bothersome because adults usually are not aware of it, unless problems arise from the amount

*Reference Nos. 5,6,9,22,25,29.

of day-dreaming that goes on. Several studies have shown a decided increase in day-dreaming when comparing pre- and post-pubertal periods.^{28,30,31} Day-dreaming is a pleasant, popular pastime and during adolescence it is purposeful in that it brings relief from outside pressures and allows for the mental rehearsal of the present and future roles the adolescent may play.

When the experimentation is done overtly—that is, either verbally or by actual activities—it can be threatening and create conflict between the teenager and the adult world. It is this process that accounts for such behavioral inconsistencies as these: Acting altruistic one moment and greedy and self-centered the next, shifting from being startlingly perceptive to blankly obtuse, being prejudiced one time and tolerant the next on the same issue, making frequent (and occasionally unrealistic) shifts in occupational aspirations, changing from mature actions to frustratingly childish ones, shifting from one philosophical commitment to another, arguing for asceticism while eating a banana split, staring fixedly down a low-cut dress while extolling the virtues of a monastic life. Much of this behavior is carried on with bewildering speed and without the adolescent's being aware of any contradiction, for it is being done with feeling, passion and purpose.

When faced with this frustrating inconsistency, adults have a tendency to err by viewing an adolescent's statement or action as being more final and permanent than it really is, and in turn reacting with anger, accusation or relief when it changes, as it usually does. In considering adolescence, it is a help to remember that the over-all purpose is serious and the end results relatively permanent but the day-to-day process is characterized by experimentation and change.

Development of self-motivation and self-determination. To accomplish this it is necessary for the adolescent to be able to rely on himself as the primary source for personal initiative and direction. With the onset of adolescence young people begin to show increasing resistance and reluctance to act when adults try to direct and oversee their behavior. Adolescents resent not being let alone to make, organize and implement personal decisions. There is a continual need for more responsibility along with demands for recognition of their growing self-reliance. They become incensed at being checked on and they feel stifled when their parents try to motivate them.

In contrast to their behavior when as children they responded relatively well to direct requests, during this period the adolescent seems to be more strongly motivated to do the opposite of what his parents or other authorities desire. If development were to stop here the task would not be completed, because at this point teenagers are not as much initiators of action as they are still responders. They are still responders because the source of motivation is still the same—parents and other authorities—the only difference being that behavior is often motivated for oppositional and negative reasons. It is only after adolescents are more fully self-motivating and not dependent on others for either positive or negative impetus, that an adult level of self determination can be achieved.

The establishment of an appropriate set of values to be used as a guide for adult behavior and the self-control to implement and adhere to the ethical system selected. In this way the individual will acquire the concepts and rules of conduct necessary to ensure his ability to live in the society as an adult. Also this task is concerned with the capacity to properly balance the expression and control of emotions. Behavior that exemplifies the attempts to accomplish this task are as follows: Passionate attachment to causes, philosophical principles and ideas, and a readiness to discuss them at length; both the commitment and the skepticism toward religion that arises at about age fourteen and a half for girls and sixteen for boys¹⁷; the need to know and question the validity of all societies' rules.

The development of empathy and the practice of reciprocity in interpersonal relationships. The ability to feel tenderness, respect and concern for others is a major step in the adolescent's emotional development. It involves being able to gain one's own ends and still not trample others' rights to do the same. The adolescent begins to appreciate people as actual individuals not just as objects to guarantee or block personal satisfactions. There is a gradual decrease of fickleness and relationships become more intimate. More time is spent in speculating on reasons for others' actions and also in genuinely trying to understand contemporaries through a process of mutual exploration.

The establishment of an appropriate sexual identity, which includes the acceptance of oneself as a sexually mature person and leads to the development of meaningful heterosexual relationships. Although this could have been included as part of

the self-concept task, it is important enough to be considered by itself. The first step is based on the adolescent's acceptance of his changed body, which is becoming adult and sexually mature. Physical changes during puberty are fairly rapid, and often the teenager is not completely prepared to integrate and adjust to the changes as rapidly as they occur. The unreadiness of adolescents to adapt to these changes often manifests itself in an unhappiness with their own physical characteristics. There is always something they obsessively wish could be changed — their complexion, weight, height, body proportions, facial features, teeth, almost anything. Related to this is the compelling preoccupation with their physical appearance; hours can be spent working out in the gymnasium, or in front of mirrors, combing hair or experimenting with makeup, and there is a noticeable increase in concern with dress.

Once secondary sexual characteristics appear, there is an intense need for physical sameness with contemporaries and there is rumination about physical normality. Both accelerated or retarded development are cause for anxiety and worry, although late sexual development is the cause of many more problems. A number of studies have confirmed that, for both girls and boys, lateness of physical maturation can result in their being exposed to quite a different socio-psychological environment and one that may have generally adverse effects on personality development.^{8,12,13,21,27}

As puberty advances, sexual drives become more urgent and there is a concomitant increase in need for sexual outlets. Primarily, these outlets are masturbation (88 per cent of males and 40 per cent of females have indicated doing so), evanescent sexual experiences during early adolescence with others of the same sex (27 per cent of males and 15 per cent of females have indicated participation) and heterosexual activities which include petting and sexual intercourse.^{14,15}

With the progression of adolescence the social and physical pressures increase, and young people are now almost compelled to work out satisfactory heterosexual relationships. This is achieved by increased contact, dating, hours of thought and discussion, sexual fantasy and physical exploration and experimentation. What has to be coped with is the reality that one has sexual appetites and, for the first time, the physical capability and opportunity for sexual relations. It is then necessary to solidify the proper sexual role by accepting

oneself as a sexually mature person who can control and yet enjoy sexual feelings.

The development of new intellectual capacities and skills. It is curious to note that with all the thought given to the emotional and physical changes, little experimental work has been done to document the changes in intellectual functions. In studying the intelligence curve, Bayley² found a rapid acceleration in the first year of life, a moderate acceleration from ages one to ten, and then a slowing of the rate for the next 15 years so that at age 25 these increments are very gradual. Piaget⁷ demonstrated that during adolescence the individual becomes capable of abstract thinking. Major authorities such as Spranger,²⁶ Lewin,¹⁸ and Kroh¹⁶ have commented on the change of the adolescents' perspective of time where past and future become differentiated, important and real. Witkin³² has also noted changes in specific aspects of basic perception in early adolescence. Other studies have shown that by the end of adolescence, intellectual functioning is very close to adult level; in fact, the qualities measured by intelligence quotient tests are at near full power by age 16.

The ability to function satisfactorily with age mates and to behave appropriately in relating to the peer group. This task is regarded as an important index of how the adolescent's development is progressing, because good achievement in this area has the highest correlation with achievement in other tasks. The influence of the peer group is very strong. Most adolescents conform assiduously, as non-conformists are aggressively sought out for rejection and ridicule by the group. To the adolescent the group is very important. Especially in our society where child and adult groups are well differentiated and where the transition period is so prolonged, adolescents have been forged into a tightly knit group of their own. Coleman,⁴ author of *The Adolescent Society*, feels adolescents have become a significant sub-culture with their own music, style of dress, language, and values. The majority of teenagers' interpersonal contact is with the sub-culture made up of their contemporaries. Thus the ability to function adequately and appropriately within it to gain the necessary social rewards is vital.

To acquire training, or be engaged in a training program that will develop the skills for achieving economic independence. The individual creates a situation so he can rely on himself for sustenance and support. It is an essential step which will en-

able him to support a family of his own. The completion of this task heralds the formal termination of adolescence.

It is obvious from this formidable and idealized list of tasks that there are large numbers of adults leaving adolescence, achieving economic and apparent emotional independence, who have yet to complete the full list. This factor explains why in our society it is not difficult to find adults of various ages who are still personally struggling with "adolescent" problems; and it also contributes to the open-ended quality of the adolescent period itself. Nevertheless, a reasonable amount of achievement in each of these tasks is necessary, because it is upon this base that the future psychological growth and maturity of the adult will be built.

Summary

This paper has addressed itself to reviewing the normal psychological development of the American adolescent. The development was outlined in such a way as to emphasize the purpose of adolescence and through this establish a basis for assessing the appropriateness and developmental level of adolescent behavior.

The developmental task concept of Havighurst¹¹ was used as a theoretical basis and nine essential tasks of adolescence were outlined. The inherent flux of adolescent behavior was made more purposeful by relating aspects of their behavior to the accomplishment of certain of these developmental tasks.

Special emphasis was given to the establishment of a self-concept, because it is considered by most authors to be the most basic task of adolescence. Experimentation, the process through which much of the emotional growth of adolescence occurs, was elaborated.

Adults who deal with adolescents were cautioned not to judge normality or abnormality by adult standards, but to view adolescence in reference to its own processes and purposes.

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Management of Transient Cerebral Ischemic Attacks

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■ *Transient ischemic attacks (TIAs) are brief reversible episodes of neurological dysfunction due to temporary focal cerebral ischemia. Angiography should be performed only when operation is indicated or when the diagnosis is in doubt. Surgical treatment is recommended when the patient is a good surgical risk, when the stenosis is more than 70 per cent in the appropriate vessel and in certain patients with less severe stenotic lesions that appear to be a probable source of emboli. Anticoagulant therapy is indicated when there are recurrent TIAs, when the patient is not a good surgical candidate and when no appropriate surgically remediable lesion is found by angiography. If there is any significant contraindication to anticoagulants they should not be given. Discontinuance of anticoagulant therapy when the patient has been symptom-free for six months is recommended. In the experience of the authors the TIA syndrome is more benign in its course than was originally suspected and a conservative approach to surgical and anti-coagulant therapy is recommended.*

IN THE WIDE SPECTRUM of strokes due to ischemic cerebral vascular disease, those manifest in the syndrome of transient cerebral ischemic attacks (TIAs) are the most challenging and provide the best therapeutic opportunities. In this report, current concepts of the pathophysiology, natural history and treatment of patients with TIAs are reviewed. Eleven case histories are included to illustrate the practical problems and decisions

involved in selecting the appropriate workup and treatment program for such patients. These cases are selected from a large series of patients from the Cerebral Vascular Research Clinic, Wadsworth Hospital, Los Angeles VA Center. During the last ten years, approximately 300 patients have presented with TIAs only.^{1,2,3} This constitutes about 10 per cent of all patients diagnosed as having ischemic strokes.

Transient cerebral ischemic attacks or transient strokes are brief, reversible episodes of neurological dysfunction due to temporary focal cerebral ischemia. Usually these episodes last only minutes to an hour, but they may occasionally persist as

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Supported in part by U.S. Public Health Service grant N.B. 03385 and by Veterans Administration research grant CN 12-58.

Submitted 24 May 1967.

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long as 24 hours. Frequently the attacks are recurrent, but it is not uncommon for a patient to have only one or two such attacks. Although vascular operations and anticoagulation may be useful in certain of these patients, the associated risks require that the clinician be judicious in the selection of patients to be so treated.

Pathophysiology

An awareness of some of the pathophysiological mechanisms underlying TIAs is important in evaluating and managing such patients. The primary abnormality common to all these patients is a transient decrease in delivery of blood to a focal area of cerebrum or brain stem. Many factors may be involved in the production of such focal ischemia. They may be categorized as local, regional and systemic. Locally the involved cerebral area may have a chronically marginal blood supply due to atherosclerotic stenosis of the major cerebral arteries or their branches or to sclerosis of arterioles directly supplying the area. A number of systemic abnormalities which may cause decompensation of such a partially ischemic area have been identified. These may include transient episodes of systemic hypotension, transitory cardiac dysrhythmia and other causes of diminished cardiac output, cerebral embolic events of cardiac origin, alterations of blood coagulation, hypoxia, hypoglycemia, polycythemia, anemia and even sudden rises in blood pressure with reactive vasospasm. Such systemic precipitating factors were identified in about 10 per cent of the TIA patients seen by us, an incidence that accords with the observations of Burrows and Marshall.⁶

Regional factors include atherosclerotic obstructive lesions within the neck vessels and, rarely, extravascular abnormalities, such as vessel kinking, fibrous bands and cervical spondylosis, which may cause intermittent mechanical obstruction of these vessels. These lesions may play a role in the production of focal cerebral ischemic phenomena, but direct proof of such a relationship is rarely available. While postmortem studies of patients with cerebral infarctions have shown a high incidence of extracranial vascular disease,^{11,13} similar changes have been noted in patients of comparable age without cerebral ischemia.²⁰ Extracranial vascular abnormalities are readily demonstrated radiographically and are frequently accessible to surgical intervention, but the clinical significance of such lesions in any individual case

is difficult to assess. Two angiographic studies of subjects without clinical evidence of cerebral ischemic disease uncovered extracranial arterial lesions in 23 per cent and 53 per cent of the subjects studied.^{5,9} On the other hand, many patients with TIAs have no demonstrable extracranial vascular lesions. Since extracranial arterial obstructive lesions may exist without symptoms of cerebral ischemia and symptoms of cerebral ischemia may occur in the absence of extracranial arterial occlusive disease, the coincidence of these two phenomena cannot be considered proof of a causal relationship. On the other hand, such a causal relationship undoubtedly exists in some symptomatic patients.

There are two ways by which extracranial obstructive lesions may cause cerebral ischemia. A decrease in the size of the lumen of the vessel may cause a reduction of blood flow distal to the obstruction. It is not commonly appreciated how severe a degree of obstruction is required to reduce blood flow. May, DeWeese and Rob,¹⁵ working with dogs, showed that an 80 per cent reduction of the lumen was necessary to reduce flow. Brice, Dowsett and Lowe⁴ demonstrated that carotid stenosis will significantly reduce blood flow only when its cross-sectional area is less than 2 square millimeters. Therefore, the presence of a stenotic lesion of an extracranial vessel, unless quite severe, would not be expected to decrease cerebral blood flow, locally or generally. The second way by which extracranial obstructive lesions may cause TIAs is by providing a source for emboli. In 1959 Fisher¹⁰ reported funduscopic observation of emboli passing through the retinal arteries during transient monocular blindness in patients with carotid artery disease. Honour and Russell¹² showed in rabbits that a series of experimentally produced platelet emboli commonly follow an identical course distally through the arterial tree. Thus, recurrent emboli might be expected to produce similar symptoms each time. Rough extracranial atherosclerotic plaques with only moderate stenosis may be a potential source of such emboli. Emboli may also arise from similar lesions of the larger intracranial vessels. The apparent salutary effect of anticoagulant therapy in many patients with TIAs is presumably due to a decrease in the frequency of such embolization as well as reduced sludging in low pressure collaterals.

Prognosis of TIA

Valid conclusions concerning the efficacy of therapy for a disease can be drawn only when there is adequate knowledge of the natural history of the disease. Since prolonged anticoagulant therapy and surgical relief of extracranial vessel obstruction are not without hazards, consideration of prognosis must influence decisions about individual patients. Only limited data concerning the natural history of patients with TIAs is available. Marshall¹⁴ reported that in a group of 61 patients presenting with recurrent TIAs who were followed an average of nearly four years, a major stroke developed in only one patient. These observations are similar to those in our own study.³ In a group of 30 TIA "control" patients followed up to eight years, only four had strokes; two of them recovered completely and two were left with mild residual effect. These studies suggest that the prognosis of this disease may be more benign than previously suspected, and this should be considered when decisions concerning therapy are made. Marshall¹⁴ reported another group of 68 patients who were seen initially with a major stroke which had been preceded by one or more TIAs. He was unable to ascertain any clinical features that would permit prediction of which patients with TIAs will eventually have major infarctions. Marshall's data on the two groups of patients should not be interpreted as evidence that over 50 per cent of patients with TIAs will eventually have cerebral infarctions. We believe that the difference between the two groups of patients is the result of the process of selection. The group of patients who present initially with TIAs alone may be viewed as similar to, say, a *prospective* study of patients with headache, who as a group have low morbidity and mortality and only rarely a brain tumor. Those presenting with a major stroke may be compared with a *retrospective* study of brain tumor cases, in which the history of headache is quite frequent. The actuarial expectation of strokes in persons who have had TIAs is as yet unknown. It is likely that many patients with one or few TIAs do not seek medical attention. Epidemiological surveys of large populations may be necessary in order to obtain this important information.

Management of TIA

The diagnosis of TIA may be clear-cut, but at times the differentiation between non-specific syncope, vestibular disorders, migraine, focal sei-

zures and TIA may be difficult. Cerebral neoplasms occasionally first come to notice through intermittent symptoms resembling those of TIA. In all patients a careful medical work-up should be performed. This should include careful auscultation of the neck for bruits and determination of the blood pressure and pulse in both arms. In certain cases significant systemic factors may be present. Hypertension, anemia, polycythemia, hypoglycemia or various forms of cardiac disturbance may be found. A reduction in cardiac output may be due to a developing myocardial infarction, angina, congestive heart failure or paroxysmal dysrhythmia. Since these conditions may themselves be responsible for the observed TIAs, treatment should be directed to the optimal management of them. Appropriate therapy for these conditions will often result in disappearance of the TIAs. Severe hypertension may also contribute to the production of TIAs. We believe that the carefully monitored gradual reduction of hypertension is an important part of management in these cases. We have seen a number of patients in which TIAs cease or decrease in number when hypertension is reduced. We do not use or recommend the use of vasodilators in the management of TIAs. There is insufficient evidence that they have value.

Indications for Angiography

Angiography is a valuable diagnostic aid in the management of patients with TIAs. However, since there is a small incidence of complications associated with this procedure, it should be carried out only when vascular operation is contemplated or when necessary to establish the diagnosis. In order to have adequate information to make decisions regarding operation, it is commonly necessary to visualize the neck vessels arising from the aortic arch. For detailed visualization of areas not seen on the study of the arch and for adequate intracranial arteriography, injection into individual vessels either percutaneously or via catheter may be necessary. A detailed discussion of the various applicable angiographic techniques and evaluation of angiographic findings is contained in Wilson's review article.²⁴

Surgical Treatment

Surgical treatment is at present available only for obstructive lesions within the extracranial vessels. The usual procedure is endarterectomy with

removal of atherosclerotic plaques with or without a patch graft to enlarge the lumen of the vessel. Various by-pass procedures are used under special circumstances. Attempts to reopen completely occluded vessels are generally unsuccessful and may be dangerous. We have found, as have others,²² that patients with evidence of severe chronic cerebral dysfunction or permanent focal motor deficit do not benefit from operation and run a higher risk of death or severe complications. At present we consider operation for stenosis of the extracranial vessels for TIA to be an elective procedure. Therefore, if a patient's general medical condition is poor, extracranial vessel operation should not be undertaken.

Vascular operation may be indicated in a patient with an accessible stenotic lesion of the carotid, innominate or subclavian arteries if the involved vessel is appropriate to the apparent location of the cerebral ischemia and if the stenosis is severe enough to cause reduction of distal blood flow. If the angiogram shows stenosis of 70 per cent or more, a reduction of that severity may be considered possible and operation may be recommended. Some investigators recommend operation for stenosis of appropriate arteries with as little stenosis as 30 per cent, based on the concept that such lesions may be the source of microemboli. Because anticoagulants may be equally effective and the surgical risks are significant, we prefer anticoagulation in this situation.

We believe that stenotic lesions of vessels not directly supplying the site of ischemia should not be operated upon if the appropriate vessel is free or relatively free of obstruction. Therefore we would not attempt to treat right cerebral hemisphere ischemia by operation on the left carotid artery, or to treat brain stem ischemia by operation on one of the carotid vessels if the vessel directly supplying the symptomatic area were relatively free of disease. On the other hand, the patient having right cerebral hemisphere ischemic attacks with angiographically demonstrated complete occlusion of the right carotid artery and severe stenosis of the left carotid artery, should be considered for left carotid operation. Such a patient has reduced collateral capability and is most apt to benefit from successful operation. Unfortunately his tenuous cerebral blood supply significantly increases the risk of the operation. Decisions in such cases are not easy to make and

require careful consideration of all pertinent factors.

Severely stenotic lesions of the origin of the vertebral arteries which are surgically accessible are seldom found and the surgical risks are greater. However, if both vertebrals are occluded, operation may be indicated for stenosis of the carotids which are providing crucial collateral supply. One other situation affecting the posterior circulation which is an indication for extracranial vessel operation is stenosis or complete occlusion of the subclavian or the innominate artery proximal to the origin of the vertebral artery, when this finding is associated with reversal of vertebral artery blood flow. This situation has been termed the "subclavian steal syndrome" and its classic clinical manifestations consist of brain stem TIA precipitated by exercise of the upper extremity on the involved side. It should be suspected in any patient with brain stem TIA and reduced pulses and blood pressure in one upper extremity.

Carotid artery stenosis is a fairly common incidental finding in patients who are completely free of symptoms of cerebral ischemia when arch studies are performed for other vascular disease problems. Likewise, asymptomatic older patients with bruits discovered over the carotids on routine physical examination commonly have carotid stenosis demonstrated by angiography. There are no data available which would support subjecting such asymptomatic patients to the risks of operation. McDowell and Ejrup¹⁶ recently reported on the benign course of patients with asymptomatic cervical bruits, confirming our own observations. If a patient with known carotid stenosis or bruit begins to have TIAs, then vascular operation or anticoagulants may be considered.

Surgical treatment has been advocated for excessive vessel kinking and for extravascular obstructive abnormalities such as anomalous fibrous bands and vertebral spondylotic spurs. We have found surgical repair indicated in only the rare case in which TIAs are precipitated by specific neck movements and where angiography confirms the transient, mechanical occlusion of the vessel.

Operations for relief of extracranial vascular obstruction entail significant risks. Because criteria for defining operative mortality and morbidity vary among reports in the literature, it is not easy to determine the incidence of complications. In addition, in many of the reports on surgical series,

patients with TIAs and those with cerebral infarctions with partial recovery are not clearly differentiated. Recent papers^{7,18,25} dealing with extracranial vessel operation in patients with TIAs report a surgical mortality of approximately 5 per cent. Another 5 per cent of patients have severe complications, such as cerebral hemorrhage or infarction, resulting in severe neurologic deficit. In our observation, these figures are optimal.

Anticoagulant Therapy

In our series the majority of patients with TIAs have not proved to be surgical candidates and only a few have had identifiable underlying systemic problems. Prolonged anticoagulant therapy may benefit these patients by reducing the incidence of platelet emboli arising from atherosclerotic plaques. Further, anticoagulants may prevent thrombus formation at the site of a stenosis and thus prevent additional reduction of distal blood flow. It is also possible that these drugs beneficially alter unknown blood coagulation factors or reduce sludging in low pressure collaterals which may have roles in the production of TIAs. Empirical clinical studies have shown that the incidence of TIAs is reduced by anticoagulants.^{3,17,19,21} There is also suggestive evidence that there is a reduction in the frequency of subsequent cerebral infarctions.^{3,21}

To avoid hemorrhagic complications, patients must be selected carefully. Liver disease, bleeding diathesis, active peptic ulcer and severe hypertension are contraindications to anticoagulants. If the patient has moderate hypertension which is readily controlled with medication, anticoagulants may be used but blood pressure should be monitored frequently. Impaired ability of the patient to cooperate, whether due to organic or psychological factors, may contraindicate the use of this therapy. We utilize warfarin and bishydroxycoumarin in the management of these patients. With careful management we have encountered no major and only a few minor hemorrhagic complications in long-term anticoagulant treatment of TIAs. Because the efficacy of anticoagulants in reducing significant morbidity among patients with TIAs remains uncertain, the use of these agents is not justified when even a relative contraindication exists.

The factors which are operative in the production of TIAs may change with time; for example, a source of emboli may disappear, a stenotic lesion

may occlude, collateral vessels may increase in size or number and coagulation factors may change. In our studies of the natural history of TIAs, we frequently observed that attacks may stop spontaneously. Therefore, lifelong administration of anticoagulants does not seem indicated. At present we recommend that treatment be maintained until the patient has been free of TIAs for at least six months. If TIAs have been reduced in number but have not disappeared, we would continue treatment. We have seen no significant rebound effect when anticoagulants are discontinued, but this phenomenon has been reported by other investigators, who recommend gradual withdrawal. If TIAs reappear after anticoagulant therapy is stopped, therapy should be started again.

Reports of Cases

The following cases are selected to illustrate some of the problems this disorder presents, the variable course of the TIA syndrome and recommendations for the management of these fascinating and challenging patients.

CASE 1.— The patient was a 66-year-old white man with a two-month history of frequent TIAs. These occurred one to two times a day, lasting for a few minutes. The episodes consisted of dizziness, diplopia, perioral tingling and quadripareisis. During the two weeks before admission to hospital, the episodes lasted up to 30 minutes. On the day of admission the patient had an episode of diplopia, left hemiparesis and numbness, which cleared in three hours. He had no significant past history. Results of general physical and neurological examinations were unremarkable. No bruits were heard and all pulses were normal. Blood pressure at the time of admission was 140/100 mm of mercury. During the stay in hospital the pressure was within normal limits. Laboratory studies including electroencephalogram, skull films and cerebral spinal fluid were normal. During the time in hospital the patient had several similar TIAs which were observed by physicians. The diagnosis was TIAs in vertebral basilar distribution.

An aortic arch study was performed in accordance with our research protocol. This showed no occlusive vascular lesions of the neck vessels. The patient was included in our anticoagulant study and was assigned, by random chance, to

the "treat with anticoagulants" category. He has been receiving anticoagulants for over two years and has had only two momentary attacks of diplopia and dizziness during that time.

Comment: We recommend that patients similar to this one with symptoms in the posterior circulation, should be treated with anticoagulants and the treatment continued until they have been free of symptoms at least six months. Because of the negligible discovery of lesions accessible to operation and the higher surgical risks involved, we do not believe angiographic studies are indicated.

CASE 2.—A 55-year-old white man, not hypertensive, experienced sudden onset of left facial weakness and dysarthria lasting 24 hours. The following day he had a second episode, very similar in nature, lasting several hours. He was admitted to hospital, where results of general physical and neurological examinations were unremarkable except for a soft bruit over the right carotid bifurcation. On the following day a right carotid angiogram showed stenosis of the right internal carotid artery intracranially in the region of the siphon. Immediately following right carotid angiography, the patient had an episode of left hemiparesis which cleared after four hours. As a part of our long-term anticoagulant study, this patient was, at random, designated to receive anticoagulant therapy. He has received anticoagulants for over four years and has had no further TIAs during this period.

Comment: At present we recommend an aortic arch study in cases of this type in which unilateral transient symptoms recur in the distribution of the carotid artery. Single vessel study, such as was done in this patient, involves more risks and might miss significant lesions in other vessels which could alter management. If the arch study showed only the carotid stenosis in the region of the siphon, which is inaccessible to operation, anticoagulant therapy should be used.

CASE 3.—An active normotensive 68-year-old white man with arteriosclerotic heart disease (three documented myocardial infarctions) had a ten-minute episode of vertigo while sitting in church. Twenty-four hours later he had a 45-minute episode of vertigo, blurred vision, paresthesias of the right extremities and weakness of the left extremities. This episode was not related to any specific movement or activity. The following day a similar 45-minute episode occurred.

He was admitted to hospital the next day. Noted on examination were blood pressure of 120/80 mm of mercury in both arms, full carotid and radial pulses on both sides, no bruits, no evidence of congestive failure or cardiac dysrhythmia, and normal neurological status. Results of routine laboratory studies including skull films, electroencephalogram and cerebral spinal fluid were within normal limits. An electrocardiogram was consistent with left bundle branch block. It was concluded that these episodes represented TIAs in the vertebral basilar distribution without clinical signs of a subclavian steal syndrome. This man was included in our study of anticoagulant therapy and, at random, was assigned to a control group. During follow-up over the next two years, with no specific therapy, this man had no further cerebral ischemic events.

Comment: This case illustrates the potentially benign course and unpredictability of this syndrome. We consider the history of significant cardiac disease in a man this age to be a contraindication for angiography and operation. This is particularly true when the symptoms are in the posterior circulation where not many operable lesions are found and the surgical risks are high. If there are no contraindications to anticoagulant therapy, this is the treatment of choice.

CASE 4.—A 59-year-old white man with emphysema, high blood pressure, arteriosclerotic heart disease and congestive heart failure, who had been taking digitalis, had two episodes of left hemiparesis and left hemisensory loss during a period of one week. One episode lasted 30 minutes and the other 15 hours. General physical examination confirmed the presence of the known diseases. There was a loud systolic bruit over the left subclavian artery, but good brachial and radial pulses were felt on the left. No significant abnormalities were noted in neurological and laboratory examinations. This patient was included in our anticoagulant study and was, at random, taken into the "treat" category. However, he changed his mind after this assignment had been made, and refused anticoagulants. During two years of follow-up he had three transient episodes of left hemiparesis, blurred vision and dizziness associated with exertion. Throughout follow-up the patient received digitalis, diuretics and a low salt diet.

Comment: Because of the seriousness of this man's other medical problems, we do not recom-

mend extracranial vessel operation. In cases in which operation is clearly contraindicated, there is no need to subject a patient to the small but significant risks of angiography. In patients with cardiac disease, especially those who have been in congestive heart failure or who have transient cardiac dysrhythmias, it is not uncommon to see cerebral ischemic symptoms secondary to diminished cardiac output.

CASE 5.—The patient, a 55-year-old white man who did not have hypertension, had ten episodes of left hemiparesis, lasting 15 to 30 minutes each, over a five-day period. These were not related to any specific activity. Results of general physical and neurological examinations were within normal limits. The blood pressure was 130/90 mm of mercury and no bruits were heard. Right carotid angiography revealed no abnormalities. This patient became, at random, a member of the control group in our anticoagulant study. During a three-year follow-up with no specific therapy, the patient had no further TIAs or other cerebral ischemic events.

Comment: Today we would perform an aortic arch study on such a patient. If no appropriate surgical lesions were found by arteriography, we would recommend anticoagulation.

CASE 6.—A 64-year-old retired ship's steward, was first seen because of complaint of recurrent 15-minute episodes of numbness of the left extremities and clumsiness of the left hand. He had had 10 or 15 such episodes during the preceding year. For three years, the patient had noted claudication of both lower extremities upon walking one block; and a year before the present examination he had had an aortographic examination at another hospital for evaluation of this problem. Bilateral iliofemoral operation had been proposed at that time but he refused. Hypertension had been present for six years and he was taking reserpine and chlorothiazide. General physical examination revealed bilateral carotid bruits and absence of femoral and distal pulses in both lower extremities. Results of neurological examination were within normal limits, as were routine laboratory studies, including an electroencephalogram, x-ray films of the skull and examination of the cerebral spinal fluid. An aortic arch study revealed severe narrowing of the right internal carotid artery to about 1 mm at its origin and mild (30 per cent) narrowing of the lumen of the left internal carotid at its origin. Pronounced obstruc-

tive disease of both common iliac arteries was also demonstrated. The patient elected not to have operation. He was then enrolled in the anticoagulant treatment study and was assigned at random to the anticoagulant treatment category. The patient has been treated with anticoagulants since December 1964 and has had no episodes of cerebral ischemia in that time. The patient has been receiving 0.5 gm of chlorothiazide daily and blood pressure has remained around 140/90 mm of mercury.

Comment: We recommend an aortic arch angiogram in this situation because of the clear-cut history of recurrent episodes of cerebral ischemia in the distribution of the right internal carotid artery plus the presence of bruits. The stenosis of the right internal carotid seen angiographically was severe enough to cause distal pressure reduction in this vessel, and therefore right carotid endarterectomy is recommended.

CASE 7.—A 63-year-old white man had five TIAs over a five-month period. Three of these episodes consisted of the sudden onset of dizziness and weakness of all four extremities, with complete clearing in one to two hours. Two of the episodes were restricted to sudden left hemiparesis which cleared within one hour. The patient was admitted to hospital and the general examination revealed blood pressure of 130/80 mm of mercury in both arms, normal retinal blood pressure and a systolic bruit over the right carotid bifurcation. Results of neurological examination and of routine laboratory studies including films of the skull, an electroencephalogram and cerebral spinal fluid examination were within normal limits. Right carotid angiography demonstrated severe (80 per cent) stenosis of the right internal carotid artery at its origin. It was our impression that this man had TIAs in the distribution of the vertebral basilar system and the right internal carotid system. In this case the patient was taken into our cerebral vascular disease anticoagulant therapy study, was assigned, by random chance, to a control group receiving placebos. During the first two years of follow-up the patient described only very occasional brief episodes of vertigo. During the next two years he reported frequent 15-minute to half-hour episodes of blurred vision, dysphagia and choking sensation. These episodes occurred as often as two or three times weekly. During the fourth year of follow-up he began to have occa-

sional five- to ten-minute episodes of visual loss in the right eye. Within three months he was having up to ten such episodes weekly and it was decided to begin anticoagulant therapy. Within two weeks after therapy was begun, the attacks of visual loss stopped and they have not returned. He has continued to receive anticoagulant therapy to the present (eight and a half years later), is working full time and is asymptomatic.

Comment: Today we would do an aortic arch study rather than simply a single carotid angiogram in such a patient. With demonstration of such severe stenosis, which very likely could cause distal blood flow reduction in the right internal carotid system, we would recommend endarterectomy. If operation were contraindicated for any reason or if the patient refused operation, anticoagulant therapy would be instituted.

CASE 8.—The patient was a 50-year-old white man with mild diabetes mellitus. On a routine yearly general physical examination, a bruit was heard over the right internal carotid artery for the first time. The remainder of the general and neurological examinations were within normal limits. No neurological symptoms were elicited. No specific evaluation or treatment was directed toward the bruit. During two years of follow-up the bruit has persisted, but the patient has remained asymptomatic.

Comment: Angiography is not recommended. We have found no evidence to support a surgical approach to an extracranial stenotic lesion in the absence of symptoms.

CASE 9.—A 51-year-old normotensive white construction laborer, while hanging curtains one evening, had sudden onset of tinnitus, tight feeling in the head, confusion, dysarthria, left-sided numbness and paresis and gait ataxia. This episode lasted six hours and then cleared completely. During the next three months he had approximately ten similar episodes lasting five minutes to an hour. Then he had an attack in which the left-sided numbness and weakness persisted for nearly 24 hours. He was admitted to hospital two days later and routine physical examination and neurological examinations revealed no significant abnormalities. Blood pressure was 125/80 mm of mercury in both arms and no bruits were heard over the neck. Results of routine laboratory studies including skull films, an electroencephalogram and cerebral spinal fluid examination were within

normal limits. The diagnosis was recurrent TIAs in the vertebral-basilar distribution. At the time we first saw this patient we were not performing aortic arch studies. The patient was taken, at random, into our cerebral vascular disease anticoagulant therapy study and was assigned to the control group. He has been observed for more than six years and during that time he has received no specific therapy. During follow-up he has had only occasional brief dizzy spells but recently he has had occasional attacks of angina. He works part time as a furniture assembler.

Comment: At present we would recommend an aortic arch study, to rule out a significant occlusive lesion of the posterior circulation accessible to operation. If angiography is not done or does not show a surgically remediable vascular situation, anticoagulant therapy should be begun. The possibility of a benign course without specific therapy is again illustrated by this case.

CASE 10.—A 69-year-old right-handed white man had experienced six episodes of right hemiparesis lasting five to ten minutes during the two months preceding hospitalization. Aphasia was present during one episode. Hypertension had been present for 15 years but the patient was not receiving therapy. There was no other significant medical history. Noted on general and neurological examinations were blood pressures of 190/100 mm of mercury in both arms, mild cardiomegaly, a loud bruit over the left carotid artery and no neurological findings. Laboratory work-up included an electrocardiogram interpreted as consistent with left ventricular hypertrophy and possible old posterior myocardial infarction. Aortic arch angiography showed complete occlusion of the right internal carotid and 90 per cent narrowing of the left internal carotid. Under general anesthesia a left carotid endarterectomy was performed without complication. The patient has been followed a year and a half and has been symptom-free.

Comment: Aortic arch angiography is indicated in this case because of the unilateral carotid distribution of symptoms. It is obvious that when one carotid artery is occluded, operation on the other carotid is more likely to result in a neurological complication than if only one vessel were involved. However, the reduced capacity for collateral flow makes relief of the partial obstruction more urgent and often worth the added surgical risk.

CASE 11.—The patient, a 63-year-old white man, suddenly became ill while standing in his living room. Vertigo, lightheadedness and visual blurring developed, with paresthesias in the left extremities, lasting a few minutes. Blood pressure was 180/90 mm of mercury in the right arm and 110/80 in the left. A bruit was heard over the right carotid artery and in the right supraclavicular region. The left radial pulse was weaker than the right and the right femoral pulse could not be felt. Aortic arch study revealed complete occlusion of the left subclavian artery and retrograde filling of the left vertebral and subclavian arteries. Bilateral carotid angiography showed pronounced diversion of the left common carotid artery flow to the distal left subclavian artery via the left external carotid artery collaterals. Left subclavian endarterectomy was performed without complications. On follow-up aortic arch study the left subclavian artery was patent. When the patient was last seen, blood pressure was 140/80 mm in both arms. He works full time as a salesman and has been symptom free for a year and a half.

Comment: In this situation aortic and carotid angiography is recommended because of the evidence for subclavian artery occlusive disease. Angiography demonstrated impairment of brain stem blood flow because of its diversion for retrograde subclavian filling. This is a relatively urgent indication for surgical intervention.

Discussion

In addition to the foregoing cases, the patient who presents with a single TIA deserves special consideration. Decisions concerning such a patient are not easy. In our experience cerebral infarction rarely occurs in patients who present with only a single TIA.²³ For this reason we do not routinely consider such patients candidates for vascular operation or for anticoagulants. Only if there is a significant cervical bruit or signs of subclavian artery obstruction do we proceed with angiography, operation or anticoagulation.

Another problem is the appearance of recurrent TIAs in a patient with a small fixed neurological deficit due to previous cerebral infarction. If the residual neurological signs are minimal, consideration for surgical or anticoagulation therapy would be the same as for the patient with TIA. A similar patient with more pronounced neurological residuum would be considered a poor surgical candidate. Our experience^{1,2} and other published

data⁸ are such that we do not at this time recommend anticoagulant therapy for the patient with a fixed neurological deficit (cerebral infarction) even though the deficit is not severe and a potential for worsening exists.

We have previously commented on the significant morbidity and mortality associated with surgical therapy. Angiography and anticoagulation also involve risks. It is therefore vital that such procedures be used only after careful assessment of all factors involved and with full knowledge of the many risks and the uncertain benefits.

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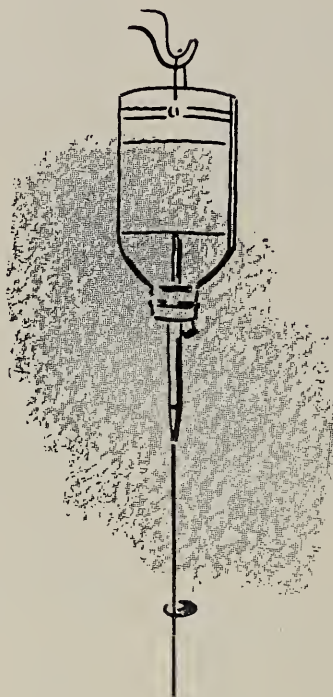
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The Epidemiology of Cancer in Animals

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■ *The principles of epidemiology are applicable to the study of the distribution and determinants of cancer in both human and animal populations. There are many examples of epidemiologic factors (host, environment, agent and time) related to cancer in animals. Certain host characteristics such as age, sex and breed are related to risk of developing cancer. Some environmental influences are illustrated by differences in the geographical distribution of certain types of animal cancer.*

Aggregations of cancer cases have been reported in herds, families and households. However, the usual distribution of cases in a population does not resemble epidemics typical of infectious diseases. Several factors (radiological, chemical, dietary, parasitic, mechanical, genetic and viral) have been identified as influences that affect the development of animal tumors.

Animal species that have been domesticated live longer and consequently malignant disease develops in more of them. Cancer incidence rates now available from data compiled by an animal neoplasm registry in Alameda and Contra Costa counties, California, indicate that some of the frequent sites of cancer in man (skin, breast and the hemic and lymphatic systems) are among the most frequent sites in dogs and cats, man's closest animal associates.

CANCER IS WIDESPREAD in nature, affecting domestic animals, wild mammals, birds and fish. Malignant lesions of similar cellular types to those observed in man are found in lower animals. Although some animals inhabit environments that

appear quite different from that of man, many exposures and disease characteristics are common to both man and animals. It is therefore of scientific importance not only to study carcinogenesis in animals in the controlled environment of the laboratory, but also to study cancer as it occurs in natural animal populations.

This report discusses some of the present epidemiologic knowledge about spontaneous neoplasms in various animal species. The traditional epidemiologic factors of host, environment and agent as well as the dimension of time are discussed as they relate to the development of cancer in animals.

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The personal studies mentioned in this communication were supported by research grant CA-05924 from the National Cancer Institute of the Public Health Service.

Part of the Special Conference on Comparative Medicine Presented Jointly by the California Veterinary Medical Association and the Scientific Board of the California Medical Association at the 96th Annual Session of the California Medical Association, Los Angeles, April 15 to 19, 1967.

Reprint requests to: State of California, Department of Public Health, Epizootology Section, California Cancer Field Research Program (CCFRP), 2151 Berkeley Way, Berkeley 94704.

Host

Cancer has been found in most animals, including such remote species as whales.¹⁴ Wild animals such as rats, that have adapted to living in human communities, also have both benign and malignant tumors. In conjunction with studies at the U.S. Public Health Service Plague Laboratory in San Francisco, McCoy⁴⁹ found tumors in 103 of approximately 100,000 wild rats examined at necropsy. Curiously, tumors rarely develop in wild house mice, although tumors are common in experimental mice of the same species as wild mice, *Mus musculus*. The literature contains only one article describing a tumor in a wild house mouse—Huebner's study,³⁵ in which a mammary tumor was found in a house mouse trapped in New York City. Andervont and Dunn³ observed that wild house mice kept in their laboratory for several generations, however, lived longer and had a wide array of tumors similar to those of laboratory strains of *Mus musculus*.

As most captive wild animals in zoos live longer than their wild counterparts, they provide a rich source of cancers for epidemiologic research. Since 1901, animals that die at the Philadelphia Zoo have been examined at necropsy.⁶⁰ Since that time, tumors have been observed in most phylogenetic families of mammals and birds kept there. The class *Aves* was less subject to new growths than the *Mammalia*. Birds had more new growths in the genito-urinary organs and mammals had more in the digestive organs. At the San Diego Zoo, an unusually large number of hepatic and biliary carcinomas developed in bears.²⁰

Recent epidemiologic research in the California Cancer Field Research Program⁶⁹ of the California State Department of Public Health has concentrated upon quantifying the incidence of tumors in domestic animals. A central animal tumor registry initiated in July 1963,²¹ derives cases

from approximately one hundred practicing veterinarians in Alameda and Contra Costa counties, California. Pet animals (dogs, cats and pet birds) make up the major proportion of animals seen by veterinarians in this area and consequently contribute the most tumors to the registry.

Preliminary analysis of cases collected in the first three years of the animal registry indicates that the incidence of malignant neoplasms in dogs and cats is high. The annual incidence rates of all cancers (Chart 1) were 381 per 100,000 dogs

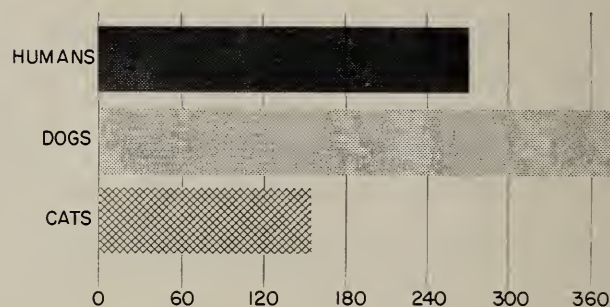


Chart 1.—Comparison of annual cancer incidence rates per 100,000 humans,* dogs† and cats† in Alameda County.

Sources:

*State of California, Department of Public Health, Alameda County Cancer Registry, unpublished data for 1960-1964, excludes skin and *in situ* cancers.

†California State Department of Public Health, Animal Neoplasm Registry, Alameda County, unpublished data for July 1963-June 1964.

and 155 per 100,000 cats compared with 272 per 100,000 humans in Alameda County.¹³ The comparison of the canine and feline rates to human rates cannot be exact because the human rates excluded skin and *in situ* cancers and were based mainly upon hospital reporting while the animal data included these cancers and were based upon cases reported from veterinarians.

Data on the most common sites in the dog and cat reported to the animal registry and on the most common sites in humans in the "Ten City Study,"²⁴ which included skin and *in situ* cancers (Table 1),

| Rank | Humans | Dogs | Cats |
|------|-----------------------|-----------------------|-----------------------|
| | | | |
| 1 | Skin | Skin | Skin |
| 2 | Breast | Mammary gland | Leukemia and lymphoma |
| 3 | Stomach | Leukemia and lymphoma | Mouth and pharynx |
| 4 | Large intestine | Mouth and pharynx | Stomach and intestine |
| 5 | Cervix uteri | Testis | Mammary gland |
| 6 | Rectum | Bone | |
| 7 | Lung | | |
| 8 | Leukemia and lymphoma | | |

*Dorn, H. F. and Cutler, S. J.: Morbidity from Cancer in the United States. Public Health Service Monograph No. 56. U.S. Government Printing Office, Washington, 1959.

†Dorn, C. R.: An animal neoplasm registry as a source of morbidity information. Proceedings of the 70th annual meeting of the U.S. Live-stock Sanitary Association, October 10 to 14, 1966, Buffalo, New York.

showed a higher frequency of gastrointestinal and cervical cancers in humans and a higher frequency of leukemia and lymphoma in dogs and cats.

The leukemia and lymphoma cases reported to the animal registry during the first two and a half years of operation have been examined in greater detail.²³ As shown in Chart 2, the annual canine

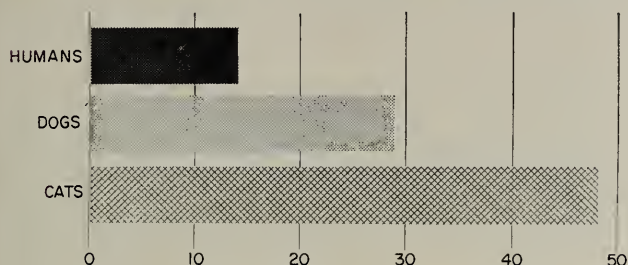


Chart 2.—Comparison of annual leukemia-lymphoma incidence rates per 100,000 humans,* dogs† and cats† in Alameda County.

Sources:

*State of California, Department of Public Health, Alameda County Cancer Registry, unpublished data for 1960-1964, excludes Hodgkin's disease and myeloma.

†Dorn, C. R., Taylor, D. O. N., and Hibbard, H. H.: Epizootiologic characteristics of canine and feline leukemia and lymphoma, *Amer. J. Vet. Res.* 28:993-1001, 1967.

incidence rate for leukemia and lymphoma is approximately twice as large as the combined leukemia-lymphoma rate (excluding Hodgkin's disease and myeloma) for man, and the annual feline incidence rate is over two and a half times as large as the human incidence rate.

Environment

Some of the relationships between environment and cancer may be shown by examining the geographical distribution of cancer cases. While cancer is global in occurrence, differences in its distribution in various areas of the world have been observed.

Horn core cancer of cattle in India is a carcinoma which develops at the base of the horn in native cattle.⁴² These carcinomas are found in cattle of some other eastern countries, but not in other parts of the world.

Bladder tumors are frequently observed in cattle in Turkey around the Black Sea.⁵⁵ These tumors have also been found in cattle of Yugoslavia, Bulgaria, Panama and Brazil. They were once common in cattle located in the northwest coastal area of North America, but now are rarely seen in the United States.⁹ They are benign and malignant tumors of both epithelial and mesenchymal origin. Only certain breeds of cattle are afflicted; the dis-

ease develops in as high as 10 to 15 per cent of cattle in endemic areas. These tumors are often found in association with another disease, enzootic hematuria, common in areas of acidic soil. The bracken fern grows in acidic soil and has been associated with chronic enzootic hematuria. Therefore, this plant has been suspected as a possible cause of bladder tumors.⁵⁵

Leukosis or lymphosarcoma of cattle is another example of varying geographical distribution. Bendixen⁸ reviewed the distribution of bovine leukosis in Europe. Before World War II, leukosis was rare in districts west of the River Elbe in Germany. Since that time, the disease has increased in western parts of Germany. This apparent spread from east to west followed the usual trade route of cattle.³⁰ If an infectious agent is responsible for this disease, it was perhaps spread with the movement of breeding cattle. Another possible means of spread, as suggested in Sweden,³³ was a viral agent present as a contaminant in piroplosmosis vaccine. Bovine lymphosarcoma has been found in many areas outside of Europe, including California.⁷⁰

The transmissible venereal tumor of dogs has been found in several countries and some areas of the United States; however, it apparently does not occur spontaneously in some populations. Only four cases were reported to the animal neoplasm registry²¹ in Alameda and Contra Costa counties, California, from July 1963 to June 1966. In all cases the dogs had been brought into California shortly before the condition was reported to the registry. The four dogs had come from Texas, Louisiana, Costa Rica and Vietnam.

Burkitt's lymphoma of man has a nonrandom geographical distribution, and histopathologically similar conditions have been described in dogs⁴⁸ and cats.⁶⁷ In man, this tumor usually affects the jaw of children and was first reported in southeastern and central Africa.¹² In Africa, this disease appeared to be altitude-dependent because it may be temperature-dependent. For this reason the mosquito was thought to be a vector of a viral agent responsible for this disease. Epstein and coworkers²⁸ successfully transplanted this tumor into African green monkeys. Dalldorf and Bergamini¹⁸ reported the isolation of a cytopathogenic agent from lymphoma cases in Africa. Several isolations of reoviruses and herpes-like viruses have been made.^{7,27,68} The etiological significance of these agents has not been determined.

Time

Neoplasms have been observed as far back as recorded history. Evidence from fossils indicates that neoplasms occurred even earlier. An osteoma of a dinosaur bone that dates back to the paleozoic period has been found.⁵³ Within more recent times, there have been secular trends in the incidence of cancer. Best known are the increase in the incidence of lung cancer and the decrease in the incidence of stomach cancer in man.

Epidemics resembling those of infectious diseases are not typical of most types of cancer. A possible exception is myxomatosis of rabbits which is usually considered to be neoplastic and which does occur in epidemics. The decided increase of lung cancer in man over the last 30 years is often referred to as an epidemic.

The term *microepidemic* has been used to describe a very small increase in incidence or several cases occurring in a relatively small geographical area in a limited period. The most notable example is the cluster of leukemia in children living in Niles, Illinois.³² Aggregations of bovine lymphosarcoma were reported in cattle herds,¹⁷ and a household cluster of feline malignant lymphoma has been observed.⁶⁴ A number of studies have shown familial aggregations of human cancer. Pinkel and coworkers reported that childhood leukemia and solid tumor cases located within a one-eighth mile radius in Buffalo, New York, also were clustered in time.⁵⁷ Application of methods developed by Ederer and coworkers to cases of poliomyelitis and hepatitis in Connecticut showed significant clustering, but cases of leukemia were not significantly clustered.²⁶ Other studies have demonstrated significant clustering in time and space for childhood leukemia in Northumberland and Durham, England,⁴¹ and in Portland, Oregon.⁵⁰

Factors in Carcinogenesis

The various agents or factors involved in carcinogenesis may be broadly grouped into the following categories: radiological, chemical, dietary, parasitic, mechanical, genetic and viral.

Radiation

Ultraviolet rays of the sun have been associated with the development of squamous cell carcinomas or "cancer eye" of cattle.² Ultraviolet radiation has also been identified as a possible cause of squa-

mous cell carcinoma of the ears of sheep in Australia.⁴⁵

During atomic testing in the Southwest, there was inadvertent exposure of a herd of cattle to radioactive fallout, and in cattle from this herd squamous cell carcinomas of the skin have developed.¹⁰ Radioactive fallout also resulted in *beta* burns in these cattle.

Chemical Factors

While there are many examples of occupational cancers of man due to exposure to chemicals, few examples exist of chemically induced tumors in animals resulting from natural exposures. Hueper, in a review of chemical carcinogens, noted the lack of examples of chemically induced tumors in animal populations.³⁷

A report based on a U.S.S.R. investigation indicated that the incidence of lung cancer is higher in dogs kept in cities than in those living in rural areas.⁴⁴ Existing data are insufficient to make a similar comparison of urban to rural canine lung cancer rates in the United States.

Observations of tumors in fish have suggested possible association with water pollutants. Carcinomas and papillomas of the lips have been found in white croakers, fish which feed off the bottom of the Pacific coastal areas.⁶² These croakers were found in waters that were contaminated by wastes from oil refineries. Papillomas have also been found in eels in the Baltic Sea and it has been suggested that the lesions may result from carcinogenic substances from industrial wastes.²⁹

Hueper,³⁶ in his book *Occupational Tumors*, cited four reports of tumors developing in animals exposed to smelter dust and fumes. Paris,⁵⁶ in 1822, observed the loss of hoofs in horses and cows kept near copper smelters and tin-burning houses in Cornwall. The contaminant was thought to be arsenic. Prell,⁵⁹ describing the Freiberg smelter in Saxony, related that precancerous warts developed in domestic animals and one deer. Nieberle,⁵⁴ also reporting about the Freiberg smelter, described adenocarcinomas of the nasal sinus of sheep in a flock that was within the dust and fume zone of the smelters.

Lead has also been incriminated as a cause of cancer in animal populations. Kilham and coworkers⁴⁰ reported a high frequency of kidney tumors in wild rats trapped at a refuse dump in New Hampshire. Five per cent of these rats had carcinoma of the kidney. Intranuclear inclusions

in the kidneys were found in nearly all of the rats. It was hypothesized that inhalation of lead in smoke from the smoldering dump fires produced the tumors. Intranuclear inclusions were reproduced by experimental feeding of lead acetate to laboratory rats. The exact relationship of the exposure to lead and the intranuclear inclusions which are sometimes indicative of viral disease is unknown.

Diet

Dietary components and contaminants have been associated with tumors of mammals and fish. In 1960, an outbreak of liver hepatomas developed in hatchery-reared rainbow trout in California and other states. Wolf and Jackson⁷¹ showed that trout fed on diets containing cottonseed meal had more hepatomas than trout fed on control diets that excluded cottonseed meal. It was later shown that hepatomas could be induced in trout by feeding aflatoxin, a metabolic product of *Aspergillus flavus*, which is a common contaminant of cottonseed meal.³¹ As was previously noted, bracken fern has been investigated as a bladder carcinogen in cattle.⁵⁵

Parasites

A favored hypothesis some years ago was that parasites caused cancer. More recent evidence has disproved some of the reported parasite-induced tumors. However, some animals' parasites have been established as the cause of certain tumors. For example, the cysticercus form of *Taenia taeniaeformis*, the cat tapeworm, was found with liver tumors of wild rats.⁶ The rat serves as an intermediate host in the life cycle of this tapeworm. Liver tumors have been induced experimentally by infecting rats with tapeworm ova.¹¹ In addition, an active factor in washed, ground *Taenia* larvae induced sarcomas in rats by intraperitoneal injection.

A nematode of dogs, *Spirocerca lupi*, has been found in physical association with esophageal sarcomas. These sarcomas are common among dogs living in the southern part of the United States where *Spirocerca lupi* infection is more prevalent. Two hundred and sixty-four of 3,148 dogs examined at necropsy at the School of Veterinary Medicine, Auburn University, Georgia, were found to be infected.⁴ In the same group of dogs, 39 esophageal sarcomas were found; *Spirocerca lupi* infection was observed in 38 of these cases.

Esophageal sarcomas were observed to be of significantly higher prevalence in hounds than in other types of dogs.

Hounds may be more genetically susceptible than other breeds, but the report concludes that hounds were at a greater risk because they have a greater opportunity to become infected. The life cycle of *Spirocerca lupi* explains why the hounds were more often infected. The eggs of the worm are picked up by a dung beetle. The intermediate host can be many different free-living animals, including chickens and game birds. The infective stage is the third stage larva encysted in the walls of the intestinal tract of the intermediate host. The infective third stage larvae in the intestinal wall are ingested by the definitive host, in this case, the dog. The larvae excyst in the dog's stomach and then burrow into the stomach wall. They then migrate through the gastric artery and the aorta to the esophagus, where the adult worms develop. Other circuitous routes are possible. Most dogs are infected while eating the entrails of dressed chickens or wild game. Hounds are more likely than other breeds to be fed the remains of birds and therefore are more often infected. There is need to determine what part of the parasite is carcinogenic and the mechanism by which it causes malignant transformation of cells.

Mechanical Factors.

Another hypothesis in cancer etiology is the mechanical induction of tumors; but, again, few of the examples have stood up to thorough investigation. The horn core cancer of cattle in India remains a possible example of a mechanically induced tumor.⁴³ These carcinomas of the horn develop after dehorning or traumatic injury to the horn by the yoke. Horn core cancer has an interesting sex distribution in that it is most frequent in steers; a few cases are found in cows, and none in bulls.

Genetic Factors

For the purpose of this discussion, the examples of genetic factors in neoplastic disease are divided into congenital influences and hereditary influences. Congenital tumors of animals include embryonal nephromas of pigs, mesotheliomas of the ox, and rhabdomyomas, rare heart tumors. A report from England¹⁶ described a very large abdominal fibrosarcoma which was present in a calf

at the time of birth. The tumor weighed 32 pounds, while the total weight of the calf was only 108 pounds.

Carcinoma or epithelioma of the eye in cattle provides an example of hereditary influences. Anderson¹ showed that the susceptibility to this disease was related to the degree of pigmentation of the conjunctiva. The variability between breeds was correlated with variability in conjunctival pigmentation. Hereford cattle, which characteristically have a white face and usually lack pigmentation of the conjunctiva, had a higher incidence of this disease than other breeds. A high occurrence of melanoma has been shown in offspring of red Duroc boars with melanomas.³⁴ Melanomas were far more common in gray horses than in horses of other colors.⁵²

Studies of dogs in Alameda and Contra Costa counties have shown that the prevalence of neoplasms is higher in purebred than in crossbred dogs.²² This observation suggests that a genetic influence associated with dog breeding practices, such as inbreeding, may affect cancer risk in dogs.

Viruses

The study of oncogenic viruses is of great current interest in cancer research. It is not the purpose of this section to discuss the mechanism of viral carcinogenesis; only brief descriptions of established viral-induced tumors in other than experimental animals are presented.

In wild animals, the Shope papilloma virus has been identified as the cause of papillomas in cottontail rabbits.⁶⁵ The original isolation was made by Dr. Shope from tumors procured from wild rabbits in Iowa. These tumors sometimes became malignant, and the virus provided a good laboratory model for studying transition from benign to malignant neoplasms.

The Shope fibroma virus, another virus of cottontail rabbits, has been classified as a pox virus while all the papilloma viruses are included in the papova group.⁵¹ The Shope fibroma virus is transmitted from rabbit to rabbit by fleas and mosquitoes.

Rabbit myxoma virus, also classified as a pox virus, causes myxomatous lesions in the European rabbit (*Oryctolagus cuniculus*) but does not produce the acute systemic disease in the American rabbit (*Sylvilagus spp.*). It has also been shown to be an arthropod-borne disease in which the mosquito is a mechanical rather than a biological

vector. Sanarelli⁵³ first described the infectious nature of this disease in 1898.

Another oncogenic animal virus, the fibroma virus of squirrels, was isolated by Kilham.³⁹ This pox virus was shown to be related to the Shope fibroma virus by cross-neutralization tests. The mosquito was also found to be a vector of the fibroma virus.

A virus isolation was made from wild mice near Brisbane, Australia; it was found to be related to the Friend mouse leukemia virus.⁵⁸ However, no neoplasms were found in these mice. Wild mice were found to be infected with polyoma virus, but they did not develop the disease because they do not live long enough or they receive passive immunity from their mothers which protects them during the first few days of life during which they must be infected in order for tumorigenesis to occur.⁶¹

The fibroma of deer has also been shown by Shope⁶⁶ to be a virus disease. Using cell-free filtrates, he was able to reproduce the disease in deer. The fibromas which provided his material were from deer in New Jersey. Fibromas have been diagnosed by the California Cancer Field Research Program⁶⁹ in deer from California's north coastal area and Yosemite National Park.

Lucke⁴⁷ has shown the infectious nature of kidney carcinomas of frogs. Two to three per cent of frogs sampled from the Mississippi Valley and the Midwest had kidney carcinomas.

In domestic animals and wild birds, chicken leukemia is an outstanding example of virus-induced tumors. There are four types of the disease: lymphomatosis, erythroblastosis, myeloblastosis and osteopetrosis. It has not been clearly established if one or several viruses is responsible for these conditions.

The bovine papilloma agent is included in the papova group of viruses.⁵¹ Papillomas are common in cattle, and it is possible to induce papillomas of horses with the bovine virus. Spontaneous equine cutaneous papillomas are also induced by a virus, as shown by Cook and Olson,¹⁵ using cell-free filtrates. The equine papilloma virus, however, will not induce tumors experimentally in cattle.

The viral nature of canine oral papillomatosis was reported by DeMonbreun and Goodpasture¹⁹ in 1932. The mastocytoma or mast cell tumor of dogs was transmitted by Lombard and cowork-

ers,⁴⁶ using cell-free filtrates, but an agent has not been fully characterized.

There have been several reports of viral activity in isolates from bovine lymphosarcoma, but none of these showed a cytopathogenic effect; however, one agent has been shown to form syncytia in tissue culture.²⁵ Jarrett,³⁸ using supernatant fluid from centrifuged cell suspensions, reported transmission of leukemia in cats.

The Yaba virus was isolated from an outbreak of histiocytomas in monkeys.⁵ Presently, this is the only known naturally occurring virus-induced tumor of primates. The simian virus 40, another primate virus, is oncogenic for hamsters, but has not been shown to produce tumors in the natural host.

Discussion

To support the hypothesis of a viral cause of human cancer, reference is often made to the many examples of virus-induced tumors in animals. However, if one examines more closely the animals that have virus-induced tumors, it becomes evident that very few are domestic animals. Almost all of the tumors induced by viruses that have been characterized are either of wild or laboratory animals. There are no malignancies of domestic animals which have been conclusively established as virus-induced except leukemia in chickens. If papillomas are eliminated, there are no established virus-induced tumors, either benign or malignant, in domestic *mammals*. While there is evidence of viral etiology of canine mastocytoma⁴⁶ and feline lymphoma³⁸ based upon transmission studies, no specific agents have yet been identified. More intensive virological studies should be pursued to further elucidate the role that viruses play in these cancers and the relationships that may exist with the human disease counterparts.

Hence, human studies are not unique in their lack of success to date in demonstrating conclusively a causal relationship between viruses and tumors other than papillomas. This is interesting in that man and the domestic animals, more than wild and laboratory animals, share the same environment and presumably some of the same exposures to carcinogens.

For epidemiologic studies of cancer in domestic animals, one of the fundamental resources is a systematic collection of cases occurring in defined populations. The many sometimes remote field

observations have greater value if they can be evaluated quantitatively to determine if they could or could not be expected by chance alone. Because of the infrequency of cancer cases of specific sites and the long periods of time needed for study, it is difficult to adequately study the distribution in time of cancer occurrence in most animal species. Some observations of varying geographical distribution of neoplastic disease based upon presence or absence of the disease are readily apparent. In order to look with greater detail at subtle differences, however, it is necessary to have complete records such as afforded by a central tumor registry.

The animal neoplasm registry in Alameda and Contra Costa counties is an initial step in providing adequate animal cancer morbidity information. Its operation, described elsewhere,²¹ parallels that of human cancer registries and provides for the first time an opportunity to compare animal and human morbidity data in the same geographic area.

It would also be of interest to compare cancer incidence in different zoos. As the occurrence of cancer in zoo populations may extend over long periods of time, zoo tumor registries that encompass complete clinical and necropsy records and detailed population information would facilitate such comparison.

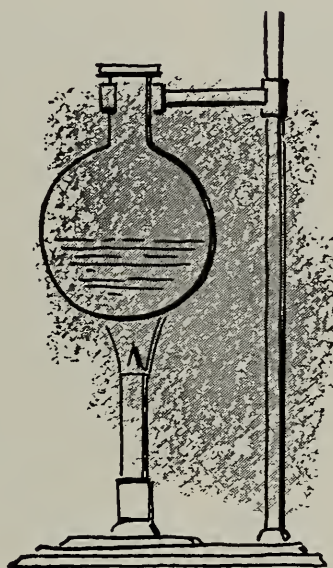
New virological, chemical, and statistical tools are needed to permit more probing etiologic studies of cancer. As scientific methods are developed to study a specific type of cancer in one species, applications to other forms of neoplasia and other animal species, including man, should be explored.

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The Short-Doyle Program

Its Past and Its Prospects

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THE COMMUNITY MENTAL HEALTH Services Act of 1957 ushered in a revolution in the provision of psychiatric services to the mentally ill, the mentally retarded and other mentally disordered persons in the State of California. The concept underlying this legislation, popularly known as the Short-Doyle Act, is that psychiatric treatment is best provided as early as possible in the course of the disorder, with the minimum disruption of the day-to-day existence of the patient.

There are several assumptions of a clinical nature implied by this concept:

- Psychiatric disability need not be either permanent or total.
- Early intensive treatment is more effective and less expensive than long-term custodial care.
- The less the life of the patient is disrupted, the more easily can the maximum social restoration be achieved.

There are also several administrative implications to the concept:

- Programs developed at the community level have a high probability of meeting the perceived needs and effectively using the available resources of that particular community.
- The ongoing development of the program is likely to be responsive to the community's changing perception of its need.
- The local administration of the program requires and reinforces the community's acceptance of the responsibility for providing psychiatric services to its members.

In brief, the Short-Doyle Act² enables communities to establish local mental health services and receive partial reimbursement of the cost from the state. Reimbursement by the state for the cost of operating such services is provided on the condition that the community meets certain requirements. A "community" is defined as a county; a city with more than 50,000 people; two or more counties; two or more cities whose combined population is more than 50,000; or a combination of cities and counties. A community can receive financial support from the state, provided at least two of the following services are included in the program:

1. Psychiatric outpatient treatment.
2. Psychiatric inpatient treatment in a general hospital or in a psychiatric hospital affiliated with a general hospital.
3. Rehabilitation services for the psychiatrically disabled to enable them to function at the best possible level socially, emotionally, vocationally, and physically.
4. Consultation by qualified mental health personnel to the professional staffs of public and private agencies and to individuals practicing privately in the community, to help them deal more effectively with mental health problems of their clients or patients before they are so severe as to require psychiatric treatment.
5. Mental health information and education services to the public and to key professional groups to build a broader understanding of mental health and mental disorders and to acquaint them with sources for help when it is needed.

Direct treatment services are provided only to persons who cannot obtain care from private

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Submitted 7 June 1967.

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sources for any reason—for example, because they cannot afford it or because it is too far away. Patients pay what they are able for treatment, but payments cannot be in excess of the cost of providing the services. Each community is required to set up a fee schedule. The Department of Mental Hygiene will advise on fee schedules, but each community establishes its own. Services are provided to those who voluntarily seek treatment and to those ordered to do so by the court. All types of psychiatric disorders can be treated—mental illness, mental retardation, alcoholism, senility, character disorders. Several methods of providing services are permissible. Contracting allows flexibility in program planning and makes possible the coordinated and effective utilization of all existing psychiatric resources. The community submits a proposed program of mental health services to the state for approval annually. The state reimburses the community for the cost of providing these services in the amount approved by the following formula:

For services which existed previously and have been incorporated into the Short-Doyle program—50 per cent.

For new services developed since the community's establishment of a Short-Doyle program—75 per cent.

The Short-Doyle Act places no ceiling on the amount of State reimbursement to a community. However, the annual total allocation is authorized by the Governor and the State Legislature and total reimbursement cannot exceed the allocation.

The State establishes the standards for community mental health services supported by state funds. It does so in consultation with the Conference of Local Mental Health Directors. The Conference consists of all regularly appointed directors of community mental health services and program chiefs as defined in the regulations. These standards encompass the quantity and quality of local mental health services; the qualification of professional and technical personnel employed; and the record-keeping procedures of each program which are relevant in terms of evaluation and fiscal responsibility.

The Growth and Scope of Short-Doyle Programs

The first programs began receiving reimbursement for services as of January 1958. Six counties constituted the initial group with approved programs. For the first half year of operation,

\$786,000 was appropriated for the fiscal year 1957-58; for the first full year of operation, 1958-59, \$1,600,000 was appropriated. Today, there are 41 approved local mental health programs.³ Of the estimated 19,000,000 population of the State of California, 16,500,000 reside in the areas covered by these 41 approved programs. Three of the programs are operated by cities or combination of cities, such as Berkeley, San Jose and the Tri-City Program in Los Angeles County. All other programs are operated as county programs. Several programs serve additional counties by contractual arrangements, for example, Sierra County contracts with Plumas County for services, and Del Norte County contracts with Humboldt County. All but 17 of the 58 counties in California have Short-Doyle programs, either by direct operation or by contractual arrangements. The counties without Short-Doyle services with the exception of three counties, San Bernardino, Riverside, and Imperial, have small populations. These three counties are the only three in the State of California with a population over 50,000 that are not participating in the Short-Doyle program. The other counties have less than 50,000 population and include such counties as Modoc, Alpine, Mono, Inyo, Trinity and others, several of which have less than 10,000 population. Alpine County has an approximate population of 400.

All programs currently approved provide outpatient clinic services and 26 of the programs provide inpatient services in general hospitals or in psychiatric hospitals affiliated with a general hospital.³ The growth in size of programs has been particularly large during the past few years. Outpatient visits have expanded as have inpatient admissions to the psychiatric units. Examples of this and comparison with state hospital admissions for the mentally ill for the last five or six fiscal years are as follows:

- For the year ending 30 June 1962, inpatient admissions to Short-Doyle programs totaled 7,445; admissions to the state hospitals for the mentally ill totaled 24,550.

- For the year ending 30 June 1967, projected admissions based on data to date indicate that inpatient admissions to Short-Doyle inpatient facilities will total 44,450 as compared with admissions of approximately 27,000 to state hospitals. Admissions to outpatient psychiatric units in Short-Doyle have increased from 15,459 for

the year ended 30 June 1962 to an estimated 84,500 for the year ended 30 June 1967. Likewise, the resident population of the state hospitals for the mentally ill has declined from 35,743 for the year ended 30 June 1962 to an estimated 23,920 for the year ended 30 June 1967.

Reimbursements by the state for 1966-67 totaled \$18,600,000. For the current fiscal year, \$23,901,030 has been budgeted for reimbursement for Short-Doyle programs. The increase in the volume of service has paralleled the increase in the number and the cost of operations of these programs.

Effect on State Hospital Admissions

Studies have been made by the Department of Mental Hygiene in an attempt to determine the effect of Short-Doyle services on state hospital admissions. This is a difficult figure to determine precisely, since many factors can influence state hospital admissions, including insurance programs which pay for private care, the effect of Medicare and Medi-Cal and other programs.

In general, we have found the following patterns: A reduction in state hospital admission rates has occurred in counties with Short-Doyle inpatient services.¹ Counties with Short-Doyle programs which do not include inpatient services but do have outpatient services have increased admission rates to state hospitals for the mentally ill; but those counties without any Short-Doyle program at all have a percentage increase in admissions to state hospitals for the mentally ill more than three times that of the counties with Short-Doyle programs that have outpatient services but no inpatient services. Specifically, counties with inpatient services in Short-Doyle show a 10.4 per cent reduction in the admission rate to the state hospitals for the mentally ill. Counties with Short-Doyle programs without inpatient services, but with an outpatient clinic show a 14.5 per cent increase in rate of admissions and counties with no Short-Doyle program at all have a 45.7 per cent increase in rate of admissions.*

The emphasis for the future, however, has to be not just in continuing what we are now doing, but in modernizing and updating and moving in new directions. For example, it is hoped the Short-Doyle Act will be revised this year, and proposals have been made to the administration

to revise the services provided from the existing five services established ten years ago to the ten services now provided in the regulations relating to the Federal Community Mental Health Center program. The proposed ten services would consist of: inpatient services; outpatient services; partial hospital services such as day care, night care and weekend care; emergency services; 24 hours a day consultation and education services available to community agencies and professional personnel; diagnostic services; rehabilitative services; pre-care and after-care services in the community; training; research and evaluation.

These ten services can provide a much broader range of service. Care could be provided for the mentally retarded on a much broader scale if these changes are made. Providing services similar to those contained in the federal regulations should make it easier for local programs to qualify for the federal staffing grants and for the federal construction funds. Utilization of the staffing grants can reduce both the county and state shares in Short-Doyle and result in considerable saving of state and local dollars. It would be possible through these revisions to submit an application for Short-Doyle which could simultaneously qualify for federal subsidy under the Community Mental Health Staffing grants.

When a local program has been able to interpose itself between a patient and a state hospital by means of a screening program before formal commitment proceedings have been instituted, or when it has been able to provide some alternative local service, the effect on mentally ill commitments has been most significant. For example, in one county in this state in 1962 there were 1,109 mental illness petitions filed and 862 commitments to state hospitals. In 1965, after initiation of a screening program, the number of petitions was 542 and there were 415 commitments. Other Short-Doyle programs with procedures for screening applications for commitment before a commitment paper is ever taken out for admission to a state hospital, have had similar experiences.

At present 26 community mental health service programs under the sponsorship of Short-Doyle provide pre-petition or pre-commitment evaluations or both for commitment to hospitals for the mentally ill. Twenty of these 26 counties provide this service for all patients committed to the state hospitals. It might be interesting to note at this point that 30 community mental health services

*The changes reported were the differences between data for a two-year period ended 30 June 1960, and a two-year period ended 30 June 1966.

under the sponsorship of Short-Doyle provide some psychiatric aftercare service to former state hospital patients. Ten Short-Doyle programs provide day treatment centers similar to those proposed for discontinuance in San Francisco, Los Angeles, and San Diego.

Programs for Retarded

Another area of interest in relation to state hospital admissions is that of retardation. Recently there has been greater interest on the part of local programs in providing services for the mentally retarded. Seven counties with Short-Doyle programs now provide some combination of screening, diagnosis, evaluation, counseling and referral services for the mentally retarded. They are Alameda County, Contra Costa County, Plumas County, San Francisco County, San Mateo County, Santa Clara County and Santa Barbara County. In some of these counties, the services include complete diagnostic services in relation to preadmission screening for a state hospital.

Considerable discussion has taken place as to the role of the Short-Doyle program in the treatment of alcoholics. Questionnaires exploring the subject of service to alcoholic patients have been returned from 23 of the 41 counties with Short-Doyle programs. The information obtained indicates that for the fiscal year ended 30 June 1966, in 12 of the 23 counties replying, more alcoholics were treated under Short-Doyle programs than were committed to the state hospital. Six of the 23 counties screened more than 50 per cent of petitions filed for commitment for alcoholism in the counties, and in 11 of the 23 counties 50 per cent of commitments to the state hospitals for alcoholism were evaluated. It should be noted that the data from these 23 programs indicated that in these programs there were 7,350 discharges of alcoholics from inpatient care and 3,242 from outpatient programs, a total of over 10,500, in contrast to 1,778 alcoholism commitments to state hospitals from these same counties in the year ended 30 June 1966.

The Future of Community Mental Health Services

The experience accumulated during the past ten years has validated the basic concept. It has also done much more. It has afforded all of us involved in providing mental health services with an opportunity to examine the total constellation of services available and how we use them.

There are gaps in service, both categorical and

quantitative. There is duplication of services. There is discontinuity of service. There is confusion as to responsibility for services. There is inadequate coordination of psychiatric, nonpsychiatric and nonmedical services. There is the all-too-human tendency for the staff in various agencies to perceive services within the limited context of their own agencies. The quality of the information upon which much of our planning is based cannot withstand scrutiny. Planning proceeds from many foci and in many directions.

These deficiencies are cited not to heap coals of fire upon the heads of those of us who have responsibility in the field but because they define the direction in which we must move. They are cited because the revolution ushered in by the Short-Doyle Act of 1957 has paved the way for a second revolution in the provision of mental health services in the State of California. We are confronted by the challenge of change generated by change. The history of mental health in California for the next ten years will be a record of how well we have met the challenge.

We can now restate the basic concept in broader terms—mental health is a community affair. A member of the community is entitled to mental health services in the same way and to the same extent that he is entitled to the other services that preserve and protect the health and welfare of the community. He should not be rejected and banished from the community as though his illness had offended God and man.

It is the responsibility of the community leaders to define the mental health needs of the community, to inventory the existing resources of the community, and carefully and systematically to plan, organize and implement a program of mental health and related services appropriate to the needs of the community. The system that is developed must be coordinated, accessible, flexible and capable of changing to meet changing need.

Our perception of the mentally ill must change. We must counteract the tendency inherent in the medical model to be primarily concerned with pathology. It is far more constructive and effective to define the resources that the patient retains and attempt to expand these to correct or compensate for his psychiatric disability. This concept flows quite naturally from the basic concept that mental illness is neither permanent or total. It casts the treatment of the mentally ill in a much more positive frame of reference and favor-

ably influences the climate of treatment for patient and staff alike. We must identify those in need of mental health services as "community patients." Our historically rooted identification of the mentally ill and disordered as "state patients" for whom the state has direct responsibility has hindered the development of community mental health services. What local mental health official would dare suggest that local government duplicate services provided by the state?

This categorization of patients often begins with commitment. Although the laws permit well-nigh unlimited discretion to the court in the matter of commitment, the extent to which this discretion is exercised is limited. This strongly suggests that some modification of the laws related to commitment is in order in those instances in which the belief that the mentally ill are a danger to themselves or society is not supported by fact.

The state responsibilities in support of the development of local programs are several:

- The first and foremost is fiscal. The taxing power of the state must be reflected in the financial support of local services. The limited local tax base makes this imperative.
- The state must continue to establish standards and ensure compliance.
- It must eliminate those direct state services in the community which it requires local services to establish.
- The state must raise the standards of staffing and services in its own institutions to the level that it demands of private and county institutions.
- It must support the continued development of programs of training, research, specialized treatment and demonstration of treatment methods in the state hospitals that are beyond the capability of small jurisdictions. It must provide bases of support in the state hospitals for local programs as pools of manpower, specialized skills and training facilities.
- It must provide continued consultation and planning assistance to local government.

There also needs to be further discussion on the question of relationship of the Short-Doyle program to the Medi-Cal program. The implications of this program for the mental health field are considerable. Considerable time and attention are being given to the relationship of these two programs with the goal of making the maximum use of both, with a minimum of conflict and confusion.

In the future, emphasis on community mental health will also be made in provision of services for crisis care, emergency care and pre-commitment screening for patients who are candidates for admission to the state hospitals. These services can considerably reduce the need for a person to go to a state hospital for treatment. It is hoped that in the not too distant future, no patient will be sent to a state hospital on a committed status unless it is determined first of all that commitment is necessary and, next, that hospital care is not available locally. Admission to a state hospital would only occur after screening by a local program or a local service and only when the necessary treatment resource cannot be provided locally.

The same concept would extend to the patients who return to the community, so that any psychiatric services a patient may require following his release from the state hospital would be provided from a local program. In this way, there would be a blending and combining of state care and local care with an continuum of services available to the patient regardless of the sources of funding, whether it be through subvention or 100 per cent state financing. This would also follow the concept and ideas envisaged in the community mental health center approach where a wide variety of services is available to the individual and these services are made available to him when he requires them, where he requires them and when he requires them, without delay, without waiting lists, whatever his age and whatever his diagnosis. A treatment program is developed to fit his requirements rather than trying to fit him into a predetermined program.

It must be noted that whereas sensitivity to local needs increases as one proceeds from the federal to the local level, administrative sophistication may tend to increase in the opposite direction. This has definite implications for program development. Further, even at the local level, governmental organization is an extremely complicated affair and program development will be decidedly influenced by the administrative structure within which it is established.

The major responsibility for collecting the data upon which such a plan for mental health services must be based is a state responsibility. A monitoring and forecasting system is required that will continuously collect data on our total mental health manpower, funding and services. This sys-

tem must record what is available, the extent to which it is utilized and the rate at which it is utilized. Criteria of effectiveness must be agreed upon, and the results of services measured against the criteria. The unit cost of the services provided must be determined and costs must be measured against effectiveness. Only when such information is available can mental health planning be conducted on a sound and systematic basis.

Much that relates to systems has been implied here and should perhaps be stated explicitly. We need to develop a systems method, applicable to the planning, operation, evaluation and continuing adaptation of a mental health services delivery system that will be comprehensive and coordinated, and will provide continuity of service and freedom of choice where applicable. The system must be community based and administered. It must be designed to meet the needs of patients. It must be pragmatic and goal oriented. Each component in the system, individual or agency, whatever its self-determined goal, must have as a su-

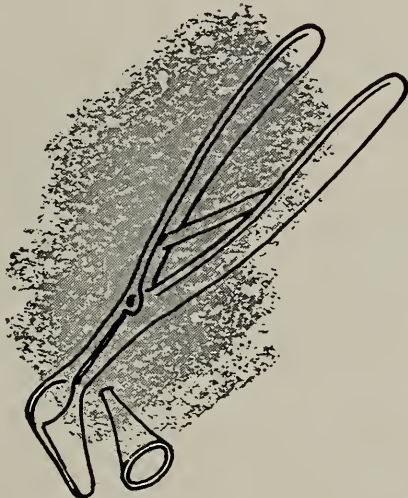
perordinate goal, the goal of the system; early intensive appropriate treatment with the maximum social restoration.

To strive for such goals might well lay one open to the charge of being idealistic. The truth of the charge notwithstanding, if we achieve them during the next ten years, we will have built well upon the accomplishments of the past ten years.

For those who find these ideas too visionary, may I offer (from *Joel*) "*your old men shall dream dreams, your young men shall see visions,*" and (from *Proverbs*) "*where there is no vision, the people perish.*"

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The Treatment and Control of Tuberculosis in California

Prospective Beneficial Effects of Medicare and Medi-Cal

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■ *Over half of all deaths from tuberculosis in California occur among elderly persons. Among the poor, prevalence is still much higher than among those in better economic circumstances. Medicare and Medi-Cal make substantial resources available but could dilute organized control efforts. Renewed professional education, cutting through fiscal intricacies, and integration of care for tuberculous persons into general medical and hospital care will maintain high standards of tuberculosis control.*

TUBERCULOSIS HAS LONG BEEN a disease falling with special severity on the poor, but its relatively high concentration among the elderly is a fairly recent phenomenon.

In 1940, more than half of all deaths among California residents attributed to tuberculosis occurred in persons less than 45 and only one-eighth in persons over 65 years of age. By 1965, the picture had just reversed: Over half of all tuberculosis deaths occurred among persons more than 65 years of age. Deaths from tuberculosis among persons under 45 years of age are becoming a rarity in California. The trend in recent years is illustrated in Chart 1.

This remarkable shift probably reflects several factors: better understanding and more effective application of control measures among younger people than among the aged; a heavier reservoir of infection subject to fatal reactivation and a

larger amount of chronic fibrotic disease among the aged. Whatever the explanation, it is clear that any substantial decline in tuberculosis mortality in California during the years immediately ahead depends upon greater efforts devoted to control of the disease among the aged.

Incidence and Prevalence

Case incidence, while not as striking as mortality, also emphasizes the importance of age. In 1940, about one-third of the newly reported cases of tuberculosis were among persons over 45 years of age; by 1965, the proportion had risen to about one-half (Table 1).

Currently in California, among persons under 45 years of age, about 30 cases of tuberculosis are reported each year for every death; among those 65 years of age and over, the ratio is only about 3 cases per death (Table 2). It appears that in tuberculosis control, as in other health services, the aged are being relatively neglected.

Evidence also confirms that tuberculosis affects the poor most heavily. For example, in West Oakland, designated as a poverty area by the State De-

The author is Director, California State Department of Public Health. Presented at a Symposium on Rational Therapy and Control of Tuberculosis, Biltmore Hotel, Los Angeles, 1 March 1967.

Submitted 12 May 1967.

Reprint requests to: Director of Public Health, State Department of Public Health, 2151 Berkeley Way, Berkeley 94704.

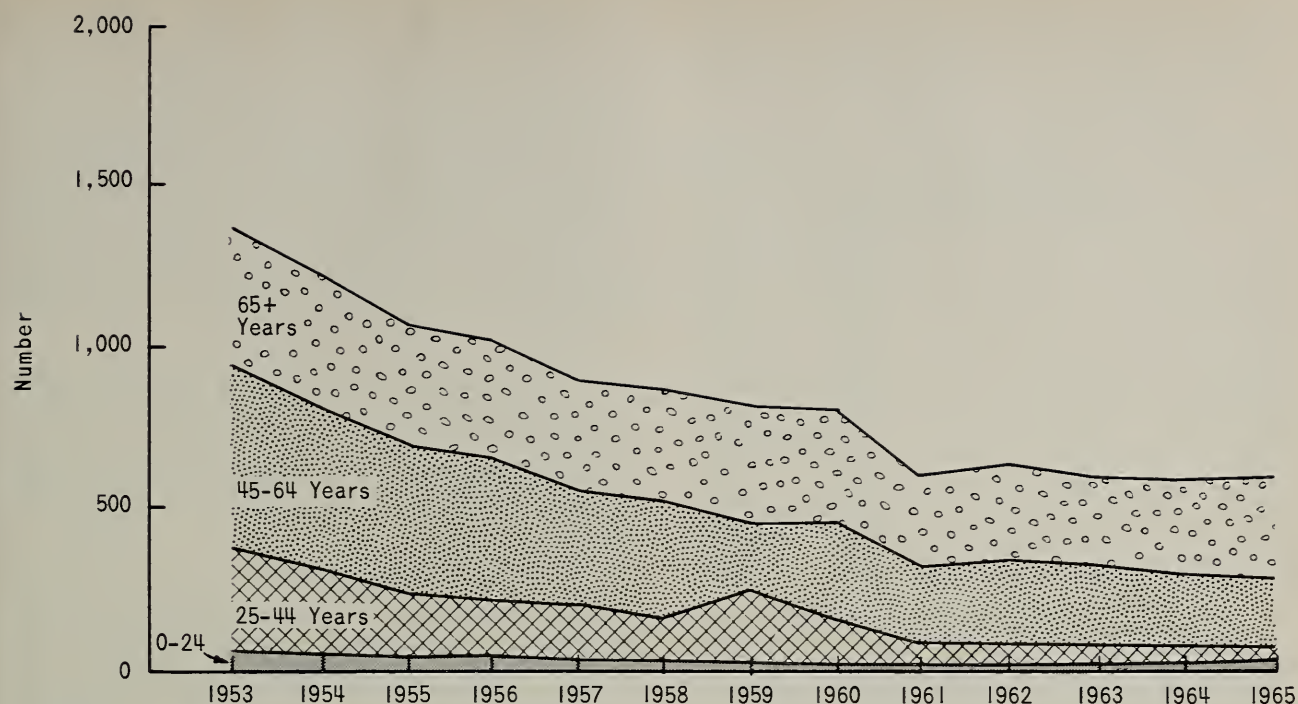


Chart 1.—Tuberculosis Deaths by Age, California, 1953-1965. Source: State of California, Department of Public Health, Death Records.

TABLE 1.—Tuberculosis Cases¹ by Age of Patient—California Residents, 1940, 1950, 1960, 1965

| Year | Total All Ages | | Under 25 | | 25-44 | | 45-64 | | 65 and over | | Age Not Stated | |
|------|----------------|----------|----------|----------|--------|----------|--------|----------|-------------|----------|----------------|----------|
| | Number | Per Cent | Number | Per Cent | Number | Per Cent | Number | Per Cent | Number | Per Cent | Number | Per Cent |
| 1940 | 7,748 | 100.0 | 2,023 | 26.1 | 3,096 | 40.0 | 2,547 | 32.9 | * | * | 82 | 1.1 |
| 1950 | 8,838 | 100.0 | 1,620 | 18.3 | 3,409 | 38.6 | 2,773 | 31.4 | 1,024 | 11.6 | 12 | 0.1 |
| 1960 | 5,566 | 100.0 | 1,092 | 19.6 | 1,593 | 28.6 | 1,836 | 33.0 | 1,043 | 18.7 | 2 | † |
| 1965 | 4,444 | 100.0 | 947 | 21.3 | 1,238 | 27.9 | 1,408 | 31.7 | 851 | 19.1 | ... | ... |

¹For 1960 and 1965, active primary cases without demonstration of tubercle bacilli are included.

*Included in age group 45-64.

†Less than 0.1 per cent.

Note: Per cents are rounded independently and may not add up to the totals shown.

Source: State of California, Department of Public Health, Morbidity Records.

TABLE 2.—Tuberculosis Deaths by Age of Patient—California Residents, 1940, 1950, 1960, 1965

| Year | Total All Ages | | Under 25 | | 25-44 | | 45-64 | | 65 and over | | Age Not Stated | |
|------|----------------|----------|----------|----------|--------|----------|--------|----------|-------------|----------|----------------|----------|
| | Number | Per Cent | Number | Per Cent | Number | Per Cent | Number | Per Cent | Number | Per Cent | Number | Per Cent |
| 1940 | 3,887 | 100.0 | 685 | 17.6 | 1,330 | 34.2 | 1,395 | 35.9 | 473 | 12.2 | 4 | 0.1 |
| 1950 | 2,301 | 100.0 | 243 | 10.6 | 633 | 27.5 | 933 | 40.5 | 491 | 21.3 | 1 | * |
| 1960 | 806 | 100.0 | 13 | 1.6 | 114 | 14.1 | 334 | 41.4 | 344 | 42.7 | 1 | 0.1 |
| 1965 | 593 | 100.0 | 17† | 2.9 | 54 | 9.1 | 213 | 35.9 | 309 | 52.1 | ... | ... |

*Less than 0.1 per cent.

†All 17 of these cases were first reported at death.

Note: Per cents are rounded independently and may not add up to the totals shown.

Source: State of California, Department of Public Health, Death Records.

partment of Finance, the tuberculosis register shows four times (220.6 per 100,000) the prevalence rate of tuberculosis that exists in the non-poverty areas of Oakland (52.0), and six times the rate in Alameda County outside of Oakland (36.5). The South Fresno poverty area, in 1966, had an incidence rate of recorded tuberculosis four

times higher (84.4) than that in the other parts of metropolitan Fresno (20.3); in the rural areas of the county the disparity was even greater. In Los Angeles, during 1965, the tuberculosis case report rate in the Southeast Health District (which lies entirely within the principal poverty area) was more than four times as high (65.8) as in the

health districts outside this district (13.1).

Table 3 lists the California counties with case rates exceeding 30 per 100,000 population.

TABLE 3.—*Counties with Case Rates of 30.0 or Higher per 100,000 Population in 1965*

| | <i>Case Rate</i> | <i>No. of Cases</i> |
|---------------------|------------------|---------------------|
| Colusa | 71.4 | 9 |
| San Francisco | 66.0 | 495 |
| Del Norte | 65.0 | 12 |
| Fresno | 51.7 | 211 |
| San Joaquin | 43.5 | 119 |
| Calaveras | 42.4 | 5 |
| Sutter | 38.5 | 15 |
| Santa Cruz | 37.6 | 39 |
| Imperial | 36.5 | 29 |
| Yuba | 35.9 | 15 |
| Merced | 35.4 | 38 |
| Butte | 33.6 | 33 |
| Nevada | 31.9 | 8 |
| Monterey | 31.6 | 70 |

(Two counties with populations under 10,000 are omitted.)

About 600 people die of tuberculosis each year in California. Increasingly, these are persons over 65 years of age, some of whom have the chronic fibrotic effects of tuberculosis. Each year, about 5,000 newly active cases are diagnosed in California, and about that number of patients (although not necessarily those with newly active disease) are admitted to beds for tuberculous patients and to tuberculosis hospitals. At any one time, approximately 2,000 patients are in tuberculosis hospitals. California's local health departments carry about 30,000 patients on active tuberculosis registries.

Impact of Medicare and Medi-Cal

Medicare and Medi-Cal emerged out of recognition that many of the aged and the poor needed more and better health care. The tuberculosis situation in California emphasizes this need. It is important to recognize that funds to pay for health care are not enough. The task of tuberculosis control still requires organization, particularly to focus efforts against the remaining pockets of the disease. The availability of money through Medicare and Medi-Cal, while helpful in some ways, may in fact make the task more complicated in other ways.

Until the advent of these new programs, California state and local governmental policy in tuberculosis control was to develop an essentially separate health care system for the victims of the disease who could not afford private care. The system consisted of county-operated tuberculosis hospitals partially subsidized by the state, and outpatient services maintained by departments of health

and some county hospitals. Health departments also carry responsibility for tuberculosis case-finding, follow-up and registry activities. (As we tighten the noose on tuberculosis, these latter activities become ever more important.) One significant aspect of the public system of care was the development and maintenance of standards for inpatient and outpatient services to tuberculosis patients, standards that were the responsibility essentially of a fairly small group of physicians.

Medicare and Medi-Cal have, in effect, changed this policy for medical care of persons with tuberculosis, in the same way that they have affected the medical care of the poor generally. The change consists of paying for services in the "mainstream" of medical care.

For almost all persons over 65 years of age, Medicare provides hospital inpatient service for tuberculosis, as well as for other conditions, for a maximum period of 90 days with some co-payment by the person concerned. It also provides organized outpatient diagnostic services. Those persons over 65 years of age who have signed up for physician services under Medicare may also obtain inpatient or office care for tuberculosis from their private physicians.

Medi-Cal, the California implementation of the federal-state medical care program for public assistance recipients, supplements Medicare in several highly important ways. For eligible persons over 65 years of age, it provides inpatient care for tuberculosis as needed — not limited to any set number of days — as well as out-of-hospital benefits. For persons under 65 years of age, however, the Medi-Cal benefit covers only 21 days in a general hospital for purposes of diagnosing tuberculosis; it does not provide inpatient care for persons under 65 years of age beyond the point of diagnosis. Medi-Cal emphasizes outpatient benefits for tuberculosis patients, providing care in county hospital clinics and private physicians' offices, as well as necessary drugs.

One early effect of Medicare and Medi-Cal is, therefore, to pay for care of many elderly and poor patients who may have tuberculosis, known or unknown, by physicians who have been accustomed to refer such patients to local public diagnostic and treatment agencies. While some physicians long experienced in tuberculosis control are concerned that this might weaken standards for care that have been carefully built up in public programs, there is no evidence as yet that this is

happening. In fact, to date, no appreciable shift from local public facilities to private physicians' offices has occurred. The latest data indicate that approximately 20 per cent of patients with tuberculosis discharged from hospitals continue to receive treatment under the care of private physicians and the remaining 80 per cent continue to get treatment through health department or county hospital clinics. This same ratio has prevailed for some years.

Challenges to Tuberculosis Workers

As the care for patients with tuberculosis becomes dispersed into the general medical community, the maintenance of high standards becomes a challenge to the physicians of the community. As usual in such a circumstance the principal responsibility falls upon those physicians, both in public service and in private practice, who are most experienced in tuberculosis work. This responsibility will have to be realized through renewed emphasis on professional education. Health officers and local tuberculosis control officers have long sought to develop in all physicians in the community a greater competence in dealing with tuberculosis. With specialized tuberculosis control projects supported in California with approximately a million dollars of federal funds each year, covering 75 per cent of the state's population, local health departments have been able to augment consultation, laboratory, roentgenographic, followup and other services to private physicians to assist them in caring for their tuberculosis patients. Reports of such developments around the state are most gratifying.

A second challenge posed by Medicare and Medi-Cal is devising the best path for tuberculosis control through the financial intricacies of these programs. The health officers of the state have decided not to press for payment for care given in their tuberculosis clinics to patients eligible for Medi-Cal, because of the present program requirement compelling a charge for similar care to patients who are not eligible for Medi-Cal. Since a large part of the tuberculosis clinic caseload consists of poor, single, middle-aged men and others not eligible for Medi-Cal, it is believed that charging such patients for their care would set tuberculosis control back.

If the \$2.8 million state subsidy for sanatorium

care were put into the Medi-Cal Health Care Deposit Fund, it would be matched by an equal amount of federal money. Here again, however, the problem of Medi-Cal eligibility requires a cautious approach. A way must be devised to cut through the regulations pertaining to eligibility and to federal-state-local financing so as to make maximum, intelligent use of these new funds to improve tuberculosis control. From the latter standpoint, the system is not entirely rational yet.

A third challenge may be even more fundamental: the extent to which care for tuberculosis should be integrated into general medical and hospital care, rather than segregated as in the past. For a variety of reasons — technical advances, changes in public attitudes and governmental fiscal policies — general hospitals are increasingly willing to accept patients with tuberculosis. This is true also of other diseases formerly treated only in separate facilities — for example, mental illness and alcoholism. This tendency raises sharply the whole question of organization of services for tuberculosis control.

In light of the declining tuberculosis problem and our changing ways of dealing with it, how long should we continue the tuberculosis sanatorium system? The answer to this question involves one important point and at least two other questions. The point is that the tuberculosis sanatoria of this state have been and still are major bulwarks in tuberculosis control. A proper conservatism implies that we should not relinquish something so useful without a sure grasp on something better. The questions are: (1) How can we assure as high a quality of care in general hospitals as that attained in the specialized tuberculosis facilities? and (2) How can we continue to make maximum use of the excellent skills developed by the highly specialized personnel in tuberculosis hospitals, both private and public? The answer to the first question may lie in gradually establishing special tuberculosis services with high standards in a limited number of general hospitals. The answer to the second may come through extending the work of tuberculosis specialists to other chest diseases. Both of these answers are now being explored in practice.

It seems imperative to maintain tuberculosis control at a high level, even higher than formerly, if we are to eradicate tuberculosis promptly, with the resources now at our command.

Hypoallergenic Breads

Wheat Content of Products Available in the San Francisco Bay Area

ARTHUR LIETZE, PH.D., ALBERT H. ROWE, M.D., AND
ALBERT ROWE, JR., M.D., *Oakland*

■ *Substantial amounts of soluble wheat antigens have been found in breads sold as "wheat-free" in the San Francisco Bay Area. Physicians with patients on a wheat-free diet are urged to exercise careful supervision over their patients' choice of such breads.*

FOR THE STUDY AND CONTROL of allergic sensitivity to wheat in humans total elimination of this grain from the diet is necessary. In addition, the initial elimination of other cereal grains is important because of their varying content of proteins identical to those in wheat and the presence of antibodies to proteins in such cereals cross reacting with wheat in the patient's serum. Breads and other bakery products made of soy or lima bean flour, potato starch, a corn starch-free baking powder, salt and water, according to our recipes⁴ in the home or by cooperative bakers, have long been used for such study in our practice.

Serious asthma or other clinical allergic disease in highly wheat-sensitive persons has occurred following the ingestion of commercial bakery products containing gluten or other wheat proteins but not so labeled. The substitution of home-made or accurately prepared commercial bakery products found by us to contain no wheat protein has resulted in the control of such wheat sensitivity disease.

From the Immunochemistry Department, Samuel Merritt Hospital, Oakland.

These studies were supported by a grant from the Charles E. Merrill Trust, Ithaca, New York.

Submitted 11 April 1967.

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Materials and Methods

To determine unlisted wheat proteins in bakery or other food products, sample loaves of bread were purchased at 14 health food stores in five counties of the San Francisco area. For purposes of this study "bread" is considered to include such products as hamburger buns but not to include cinnamon rolls or the like. A sample of each loaf purchased was allowed to dry in the air at room temperature. One gram of each dry sample was then extracted for 24 hours at 4°C with 10 ml of isotonic saline solution.

Standard solutions of wheat antigens were prepared by similarly extracting 1 gm of wheat flour, commercial gluten flour and gluten* with 10 ml of saline solution each.

Reagents

Saline. Nine volumes of sodium chloride solution, 8.8 gm per liter, were mixed with 1 volume of phosphate buffer, 32.7 gm $\text{Na}_2\text{HPO}_4 \cdot 7\text{H}_2\text{O}$ and 4.0 gm KH_2PO_4 per liter.

Antibody. Four rabbits were each injected intramuscularly with 1 ml of standard wheat flour suspension weekly for seven weeks, rested five weeks and reinjected. One week later they were

*Nutritional Biochemicals Corporation, Cleveland, Ohio.

bled and the serum obtained. The highest titer serum, as judged by precipitin tests, was used for these experiments.

Antibody Specificity

These sera contained no antibody to materials other than wheat or rye which might legitimately be present in these breads. Other cereal grains tested, with completely negative results, include extracts of oats, corn (*Zea mays* seed), rice, millet and wild rice. Barley, rye and sorghum seed extracts yielded lines with these sera but only the reactions with barley were strong enough to cause confusion, the rye and sorghum reactions being very weak. Authentic 100 per cent rye bread gave a reading of 3 per cent "wheat flour" by this technique. As may be seen, however, from Figure 1, the slope of the calibration curve becomes so steep below 10 per cent wheat flour that figures of less than 10 per cent are almost meaningless. In any case no labels on any of these breads implied in any way the presence of barley or sorghum, which must therefore be considered

adulterants if they should be present. The conclusive check on specificity of the anti-wheat sera (at least for this purpose) is that authentic samples of wheat-free bread which contained the same ingredients as were listed on the contaminated breads yielded no Ouchterlony or radial diffusion bands with the sera.

Radial Diffusion Plates

For carrying out analyses by a modification of the radial immunodiffusion technique of Mancini and coworkers,^{1,2} vessels were prepared by cementing 9 cm diameter plastic rings to a pane of glass. To 5 ml of 3 per cent agar at 60°C was added 5 ml of rabbit antiserum to wheat at 50°C. After thorough mixing, the solution was poured into one of the radial diffusion vessels. When the gel had hardened, holes 4 mm in diameter and 12 mm between centers were punched in it in a hexagonal pattern. Each sample extract was used to fill one of these wells. It is important that the meniscus be neither convex nor concave but as flat as possible. The standard solutions were each diluted 1:3, 1:10, 1:30, 1:100 and 1:300, and each dilution was used to fill one well.

The plate was put into a humid chamber at room temperature and allowed to develop for 24 hours. At this time the diameters of the circles of precipitate around each hole were measured and recorded. The plate was then washed with five changes of saline solution, 24 hours at room temperature for each wash. After the last wash, the plate was stained with 1 per cent Buffalo black in 5 per cent acetic acid for 30 minutes. The stained plates were then washed repeatedly in 2.5 per cent acetic acid until the excess dye was removed. Final readings of the diameters were then taken (Figure 1).

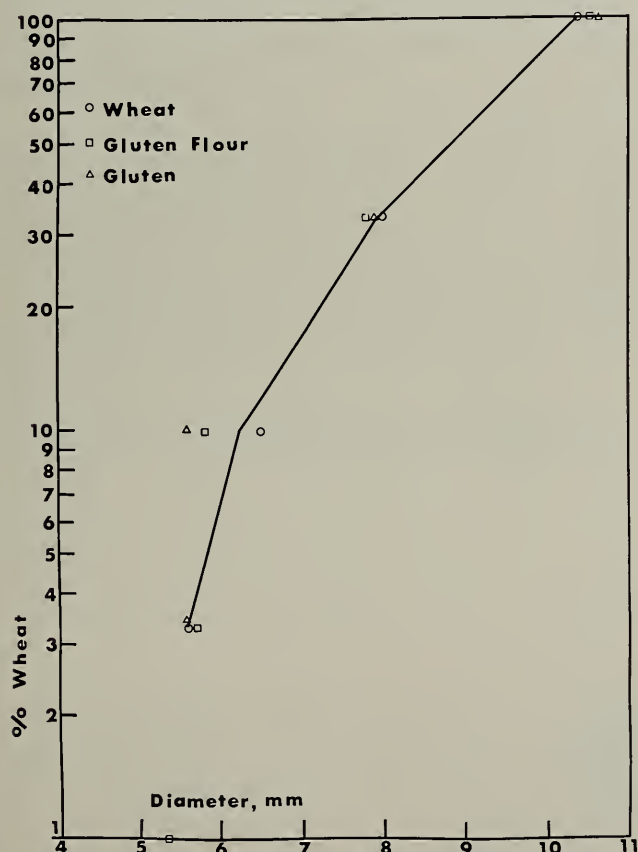


Figure 1.—Radial Diffusion Analyses, Standard Curve. Soluble antigens in bread expressed as per cent wheat flour, versus diameters of circles of antigen-antibody precipitates. Standard antigens: wheat flour, gluten flour and gluten (NBC).

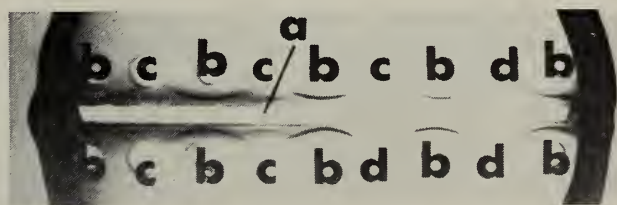


Figure 2.—Typical Ouchterlony Plate. The contents of the wells are: a. Antibody to wheat (in trough); b. Extract of known wheat; c. Extracts from "wheat-free" breads containing 10 per cent or more wheat flour by radial diffusion measurements; d. Extracts from wheat-free breads containing no significant amount of wheat flour by radial diffusion measurements.

TABLE 1.—Measurements of soluble wheat antigens, as percentage content of wheat flour in "wheat-free" breads*

| Soy-Potato and Lima-Potato Breads (10 loaves) | Other "Wheat-Free" Breads (Rice, Millet, Rye, etc.) (9 loaves) |
|-----------------------------------------------|----------------------------------------------------------------|
| 72 per cent | 48 per cent |
| 37 | 34 |
| 25 | 17 |
| 22 | 16 |
| 19 | 15 |
| 14 | 9 |
| 13 | 3 |
| 11 | 0 |
| 0 | 0 |
| 0 | |

*Since it can not be established in what form (wheat flour, high-protein wheat flour, gluten flour, etc.) the soluble wheat antigens became incorporated in the bread, the results are expressed as percentage content, on a dry weight basis, of wheat flour which would be necessary to produce the readings obtained.

Ouchterlony Plates

Vessels made by cementing plastic rings to a pane of glass were also used for double diffusion studies by a modification of the method of Ouchterlony³ (Figure 2).

Results

Laboratory

Percentages of wheat flour found in breads, as calculated from measured ring sizes by use of the standardization curve of Figure 1, are shown in Table 1. Of ten loaves of soy-potato and lima-potato bread, eight contained soluble wheat antigens corresponding to more than 10 per cent wheat flour in the bread, up to a maximum of 72 per cent. Of nine loaves of other breads labeled and sold as "wheat-free," five contained soluble wheat antigens corresponding to more than 10 per cent wheat flour in the bread.

Ouchterlony plate results (Figure 2) confirmed the occurrence of wheat antigens demonstrated by the semi-quantitative radial diffusion method. The absence of one wheat antigen in these breads in the presence of other wheat antigens, as shown by lines of identity, suggests that the adulterant may be gluten, or some other product of wheat, rather than wheat flour.

Clinical

In the past two years 15 of our patients whose symptoms were well controlled by the elimination of wheat and other foods had reactivation of clinical allergic symptoms after eating a commercial bread sold as being wheat-free. Wheat was demonstrated in these breads by the immunologi-

cal techniques described in this article. When bread and bakery products shown to be wheat-free in our laboratory were resumed, the symptoms were controlled in four to eight days.

Discussion

The radial diffusion technique used in the present study can properly be used for exact quantitation only if the antiserum is monospecific for one and only one antigen in the test extracts. We have been unwilling to adhere to this requirement, and hence the percentages of wheat flour reported here can be considered only as guides to the extent of adulteration rather than as high precision measurements.

When an antiserum reacting with several substances in the wheat is used, each substance in the wheat can be postulated to react separately with its own antibody, resulting in not one ring around the antigen well, but in several concentric rings. It then becomes necessary to select one ring in particular for the measurements and use only it. For this work we selected the outermost ring, relying on pattern recognition to ensure that it corresponded to the same antigen in every case. Fortunately, calibration curves with wheat flour, gluten flour and gluten were indistinguishable on this basis (Figure 1).

Any errors possible result from breakdown of the postulate of separate antigen-antibody reactions and from errors in pattern recognition. These causes can lead neither to finding wheat where it does not exist nor to gross errors in measurements. If a sample of bread were contaminated with some wheat product (for example, gluten, gluten flour or wheat starch) which did not contain the usual proportion of the antigen normally present in the outer ring, the next ring in would become the outer ring, and if it were read as the outer ring, the per cent wheat flour equivalent found would be too low—that is, errors from this source would cause the bread to appear less contaminated than it really was.

If a monospecific antiserum were used, it could detect only one of the many antigens present in wheat. Adulteration with a wheat preparation (such as gluten) which did not contain this one antigen could then not be detected with this serum. That situation would be tolerable if all wheat-sensitive patients were sensitive only to one and the same antigen. We have evidence that, unfortunately, this is not the case. We have found anti-

bodies in sera of wheat-sensitive and food-sensitive patients to antigens as diverse as gluten, wheat globulins and even wheat starch. It is entirely possible, therefore, that of the various soluble antigens detectable by this technique, some patients are sensitive to one, and other patients to others. For this reason we elected to use wheat antiserum reacting to many wheat antigens and to forfeit the higher precision attainable by use of monospecific antibody.

Our findings are quoted to two significant figures (of which the last figure is uncertain, in accordance with standard practice) only. For establishing whether or not the contaminant is a trace contaminant or a major adulterant, this is sufficient precision. In order to avoid implying more precision than exists, figures are given as percentages of wheat flour equivalent present in the bread rather than as milligrams of antigen per milliliter.

Clinical

The presence of large amounts of wheat in commercial "wheat-free" breads has been demonstrated by radial diffusion, by Ouchterlony tests, and by clinical responses of wheat-sensitive patients eating them.

Both medical profession and lay public must realize that bakery and other food products sold as being wheat-free may contain gluten and other wheat proteins in spite of labeling to the contrary. The ingestion of such products by wheat-sensitive patients will frequently reactivate or perpetuate symptoms due to wheat allergy. Furthermore, the unsuspected ingestion of gluten* or other wheat

*This technique is incapable of showing pure gluten, which is insoluble in saline solution. However, all commercial gluten we have examined has soluble wheat proteins contaminating it (Figure 1).

proteins in these products will prevent the relief of coeliac disease and nontropical sprue when gluten is the cause.

There is no objection to adding wheat proteins, including gluten, to food products provided such proteins are printed on the label and the products are not sold as being wheat-free.

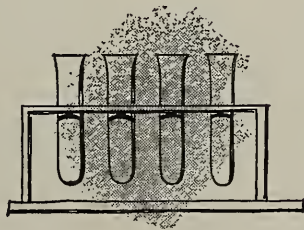
The physician can suspect the presence of wheat in a commercial bakery or food product if clinical symptoms arise after the ingestion of the product by a symptom-free wheat-sensitive patient.

It can also be determined by our immunological technique for the estimation of wheat proteins in food products. This technique can also be used to determine proteins of other foods in commercial products.

These studies emphasize the necessity not only of accurate labeling, but also of listing every ingredient in commercial bakery and other food products. To be certain that such products contain no wheat, patients should make them at home according to prescribed wheat-free recipes or should buy them from bakers who are making them by such recipes and who are supervised by the physician.

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Postpartum Sterilization

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■ *Postpartum sterilization in California is characterized by an absence of legal definition, by variations in the practices within communities and by differences of opinion as to the merits of alternative procedures. In one institution there seems to be good reason to stress postpartum tubal sterilization as being a safe and effective method of dealing with a group of patients for whom subsequent pregnancies carry a high risk. In other hospitals sterilization policies will vary according to local circumstances and needs.*

POSTPARTUM TUBAL STERILIZATION is affected by a variety of conflicting medical, legal, administrative and social considerations. There are differences of opinion as to the merits and risks of alternative methods of sterilization.^{2,5,6,8} The legality of this procedure has not been clearly defined, either on state or national levels. Within communities, there is a lack of uniform practices, and there are conflicts within and between various medical organizations and agencies. And finally, there is an ever-increasing public interest in programs for family planning and population control.

In California, there are no statutes either granting or denying the request to perform or have performed a sterilization operation outside of a state institution. In a recent opinion, the legal counsel for the California Medical Association stated that California courts would most likely hold that an operation to produce sterility, when necessary for therapeutic reasons, may lawfully be performed. On the other hand, sterilization without a therapeutic indication could constitute the crime of mayhem. It was the advice of counsel

that California physicians should not perform sterilization operations unless therapeutically indicated.

Within communities there are variations in sterilization practices. This is illustrated by an informal poll of 15 hospitals in the Los Angeles area. The majority of these hospitals have sterilization committees. Some do not. These hospital committees may or may not require formal approval of all requests for sterilization. In some hospitals, socio-economic indications for sterilization are acceptable—usually along the lines recommended by the Manual of Standards of the American College of Obstetricians and Gynecologists. Other hospitals require that a medical indication be present, and some hospital committees tend to influence methods of sterilization by their advocacy of one or another type of procedure.

It is evident that the practices of one group or in one area will be influenced by a number of factors, including social, economic, religious and professional considerations. This paper deals with only one situation as encountered in a large urban general hospital.

At the Los Angeles County General Hospital, there were 10,793 births during the fiscal year 1965-66. In the same period, 490 mothers were sterilized, either at the time of cesarean section

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Chairman's Address: Presented before a Joint Meeting of the Sections on Obstetrics and Gynecology and General Practice at the 96th Annual Session of the California Medical Association, Los Angeles, April 15 to 19, 1967.

Reprint requests to: Department of Obstetrics and Gynecology, U.S.C. School of Medicine, 1200 North State Street—Box 96, Los Angeles 90033.

TABLE 1.—*Sterilization Procedures Used in a Period of One Year*

| | |
|------------------------------------------------------|-----|
| Postpartum tubal sterilization at patient's volition | 205 |
| Postpartum tubal sterilization on medical indication | 27* |
| Tubal sterilization at cesarean section | 208 |
| Section, hysterectomy | 49 |
| Therapeutic abortion | 1 |
| Interval tubal sterilization | 0† |
| Total | 490 |

* See Table 2.

† See Text.

TABLE 2.—*Tubal Sterilization for Medical Indications*

| | |
|------------------------------|----|
| Heart disease | 7 |
| Diabetes | 8 |
| Sickle cell disease | 2 |
| Polycystic kidney | 2 |
| Pulmonary tuberculosis | 1 |
| Systemic lupus erythematosus | 1 |
| Severe asthma | 1 |
| Hodgkins disease | 1 |
| Subarachnoid hemorrhage | 1 |
| Carcinoma thyroid gland | 1 |
| Severe hypertension | 1 |
| Previous cesarean section | 1 |
| Total | 27 |

or in the immediate postpartum period (Table 1). The ratio of sterilization to delivery was 1:22 and the ratio of postpartum tubal sterilization to delivery was 1:47.

Postpartum Tubal Sterilization

Postpartum tubal sterilization is divided into two groups—medically indicated and voluntary. By medically indicated is meant that the patient had a medical disease which clearly increased the risk of subsequent pregnancy (Table 2). The term "voluntary tubal sterilization" implies that socio-economic considerations are involved and that the decision is based on a combination of age and multiparity. The concept of voluntary sterilization has achieved the recognition and approval of many groups—particularly the American College of Obstetricians and Gynecologists. It is the recommendation of the college that voluntary sterilization be permitted if the woman is over 25 and has five living children, is over 30 and has four living children, or is over 35 and has three living children.³

In the Los Angeles County General Hospital, the definition of voluntary tubal sterilization is more stringent. As a prerequisite to sterilization, following delivery, the patient must have born eight children if under age 30 or six children if older. It is our opinion that patients in this group also have medical and obstetrical indications for

sterilization because to them the risk of future pregnancy will equal or exceed the risk of the sterilization procedure.

In California, increasing age is a factor in pregnancy risk. Twenty-five per cent of the maternal deaths occur in a group of patients 35 years of age or older delivering only 10 per cent of the liveborn infants.⁴ Among the patients undergoing voluntary sterilization in this hospital, 79 per cent have a history of either a significant medical disease or complication of pregnancy. Pregnancy complications include hemorrhage sufficient to require transfusion (26 per cent), urinary tract infection (29 per cent) and toxemia (58 per cent).

During 1965, there were 16 maternal deaths at the Los Angeles County General Hospital (Table 3). It is significant that nine of the sixteen patients with a total of 65 surviving children could have qualified for voluntary sterilization under the recommendations of the American College of Obstetricians and Gynecologists. Moreover, six of these nine patients had not desired to be pregnant, as was evidenced by the fact that the cause of death was sepsis following induced abortion.

In our experience, postpartum tubal sterilization has been a safe procedure. In the three-year period ended with February 1967, there had been no mortality following 746 operations. To date, no patient has returned with pregnancy, either uterine or ectopic, because of operative failure. (Admittedly, however, pregnancy can occur years later.⁷) Operative morbidity has been less than 1 per cent, and even then consisting of either a superficial wound abscess or a small hematoma.

The type of operation, anesthetic and day of

TABLE 3.—*Maternal Deaths in the Year 1965 at Los Angeles County General Hospital*

| Age | Parity | Cause of Death |
|-----|--------|----------------------------------------------|
| 37 | 8 | Cerebral hemorrhage—eclampsia |
| 37 | 7 | Postoperative hemorrhage—tubal pregnancy |
| 30 | 7 | Ruptured uterus—oxytocin induction |
| 27 | 7 | Septic abortion—septic shock |
| 34 | 6 | Septic abortion—hypertensive disease |
| 27 | 5 | Septic abortion—pulmonary embolus |
| 26 | 5 | Septic abortion—tetanus |
| 36 | 4 | Septic abortion—septic shock |
| 29 | 4 | Eclampsia—aspiration of vomitus |
| 30 | 4 | Septic abortion—shock |
| 37 | 3 | Septic abortion—pulmonary embolus |
| 19 | 1 | Suicide—barbiturate overdose |
| 20 | 1 | Probable pulmonary embolus |
| 29 | 1 | Diabetic keto-acidosis |
| 30 | 1 | Acute purulent meningitis |
| 35 | 1 | Induced abortion—hypertensive encephalopathy |

TABLE 4.—*Data on Postpartum Tubal Sterilization, 232 Cases*

| | |
|-------------------------------------------------|-----|
| A. Type of Operation | |
| Pomeroy | 227 |
| Irving | 2 |
| Fimbriectomy | 3 |
| Cornual Resection | 0 |
| Associated with repair of incisional hernia.... | 4 |
| B. Anesthetic | |
| Spinal | 149 |
| Epidural | 9 |
| Inhalation | 52 |
| Local | 22 |
| C. Postpartum Day | |
| Delivery | 6 |
| 1 | 67 |
| 2 | 113 |
| 3 | 38 |
| 4 | 6 |
| 5 | 2 |

operation in 232 cases done during the year 1965-66 are listed in Table 4. Although the Irving operation is more certain, it was seldom done. The appeal of the Pomeroy procedure would seem to be its ease and simplicity. Local anesthesia, when employed, proved adequate—even though the patient usually experienced a certain amount of discomfort.

Now that more effective contraceptives are available, the question can be asked: Is tubal sterilization necessary? At this time, neither oral contraceptives nor intrauterine devices have provided a complete answer to the problem of family planning. This is particularly true in those areas where socio-economic factors limit the availability of medical care. An examination of Tables 5 and 6 demonstrates that there is con-

TABLE 5.—*Data on Use of Intrauterine Device in the 1965-66 Period by Patients for Whom Method was Recommended*

| | |
|----------------------------|-----|
| Method continued | 346 |
| Method discontinued* | 62 |
| Lost to follow-up | 46 |
| Failed appointment | 204 |
| Total | 658 |

*Includes three patients pregnant with device in place and three patients planning another pregnancy.

TABLE 6.—*Data on Use of Oral Contraceptives in the 1965-66 Period by Patients for Whom They Were Recommended*

| | |
|----------------------------|-----|
| Method continued | 321 |
| Method discontinued* | 127 |
| Lost to follow-up | 171 |
| Failed appointment | 104 |
| Total | 723 |

*Includes three patients planning another pregnancy.

siderable interest in contraceptive methods among our patients, but also a high rate of failure—even if it is assumed that a large proportion of patients who are lost to follow-up, or who have not kept their initial appointment, are obtaining adequate contraceptive advice from other sources.

The reasons for discontinuance of oral contraceptives by the patient were side effects (62 instances), request of the patient or her husband (62), or contemplated sterilizing surgical procedure (3). Intrauterine devices were discontinued because of expulsion (24 cases), cramps (12), bleeding (4), infection (2), patient request (6), surgical procedure (3), pregnancy (3) and miscellaneous (8). In the two groups, a total of six patients discontinued contraception because of a desire to become pregnant. Not infrequently, the discontinuation of one method was not followed by the substitution of another method. The following case furnishes a dramatic illustration.

A 27-year-old Caucasian was given an oral contraceptive following the birth of her eighth child. After 12 weeks of taking the contraceptive it was discontinued because of leg pain. Thrombophlebitis could not be ruled out. Six months later the patient was admitted to this hospital in septic shock as a result of an induced abortion. Within 48 hours she was dead, despite intensive therapy.

Sterilization at Cesarean Section

In the fiscal year 1965-66 there were 667 cesarean sections at the Los Angeles County General Hospital. Two hundred and fifty-eight of the patients were sterilized, 208 by tubal ligation, 49 by hysterectomy done in the absence of gross uterine disease, and one done on the indication of rupture of the previous cesarean section scar. This last patient is excluded from the group upon whom operation was done primarily for the purpose of sterilization.

It has been our practice not to advise sterilization with less than three children unless the patient has a serious disease or is over 40 years of age. The choice of operative procedure is influenced by the patient's age, the operative findings and the preference of the operator. While hysterectomy was more often selected for older women, the decision was not consistent (Table 7). In some cases, hysterectomy was done for very young persons, and tubal ligation was done for women approaching the menopause.

Hysterectomy has both advantages and disadvantages. The principal advantage is the removal

TABLE 7.—Data on Sterilization at Cesarean Section

| | <i>Tubal Ligation</i> | <i>Hysterectomy</i> |
|----------------------|-----------------------|---------------------|
| Average age | 30 | 32 |
| Age range | 19-45 | 22-42 |
| Age 30 or more | 50 per cent | 68 per cent |
| Parity | 4.6 | 4.7 |
| Negro | 50 per cent | 32 per cent |

of a potentially troublesome and presumably functionless organ. The major disadvantage, aside from psychological considerations,¹ is an increased operative risk. In our experience, both operative morbidity and mortality are significantly increased when hysterectomy is selected instead of tubal sterilization. During the past 15 years, the complications encountered in this hospital that can be attributed to this operation include uretero-vesical fistula, vesico-vaginal fistula, extensive hematoma, vault abscess, postoperative hemorrhage and an increase in post-transfusion hepatitis.

Other Procedures

In the period covered by this report, there were no interval (late) tubal sterilizations. However, vaginal hysterectomy was selected rather than tubal sterilization for a half dozen patients because

of associated genital prolapse. The one therapeutic abortion (and hysterectomy) was also the only therapeutic abortion performed during this one-year period. The indication for abortion was disseminated lupus erythematosus, and the patient was dead four months later.

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Benign Thymoma and Selective Erythroid Aplasia of the Bone Marrow

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■ *The occurrence of red cell aplasia of the bone marrow and benign thymoma is a rare but well-defined syndrome. Data presented suggest the presence in the serum of a patient who had thymoma, of a humoral factor which may inhibit erythropoiesis. Further attempts should be made to clarify the association of thymoma and anerythroid anemia.*

THE ASSOCIATION OF anerythroid anemia and benign thymoma emerged more than a decade ago as a clinical and pathological entity. Jacobs and coworkers in 1959 reviewed the literature and reported observations on two additional patients with this syndrome.² Serum obtained before thymectomy from one of these patients was used in an attempt to suppress erythropoiesis in laboratory animals. It is the purpose of this paper to present supplementary data from this experiment.

Method and Results

Serum obtained preoperatively from patient No. 2,² who responded to thymectomy, was stored at -10°C . The reticulocyte level in the peripheral blood of each of two groups of six weanling rats was determined daily during a five-day control period by the method described by Wintrobe.⁴ Each determination was repeated three times and the mean value determined. Subsequently, each animal in the control group was given 1 ml of normal human serum by tail vein each day for five days, and the animals of the experimental

group received the same amount of serum (1 ml per day) from patient No. 2 during the same period. Daily reticulocyte levels were determined on days four and five, and on day six after cessation of the serum injections (Table 1).

During the control period there was no statistically significant difference between the reticulocyte levels of the experimental and the control groups of animals. On the fourth and fifth days of injection, reticulocyte levels in the experimental animals decreased below control levels; the difference was statistically significant by t-test only to $p < 20$ per cent. However, on day six the difference between reticulocyte levels in the animals injected with the patient's serum and in those of animals injected with normal serum was greater ($p < 2$ per cent).

Discussion

The association of anerythroid anemia and benign thymoma emerged as a clinical and pathological entity between 1950 and 1960.² The occasional complete remissions of anemia after thymectomy suggested a causal relationship between the thymoma and this form of anemia. An attempt to demonstrate a humoral factor that would depress erythropoiesis was considered inconclusive. Since 1960 there has been a wealth of clinical information documenting the association of

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Supported in part by the A. L. Hobson Memorial Fund of the University of California.

Submitted 10 August 1967.

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TABLE 1.—Mean Reticulocyte Levels in Rats Injected with Serum from a Patient who Had Thymoma and from a Normal Human Control

| | Day 4 (Injected) | | Day 5 (Injected) | | Day 6 | |
|-----------------------------------------------------|------------------|---------|------------------|---------|---------|---------|
| | Control | Patient | Control | Patient | Control | Patient |
| Reticulocytes in Blood of Six Rats (per cent) | 11.8 | 8.1 | 5.8 | 8.0 | 8.4 | 3.6 |
| | 8.4 | 7.8 | 8.0 | 4.0 | 17.6 | 6.0 |
| | 12.3 | 10.0 | 13.1 | 5.0 | 11.2 | 5.4 |
| | 9.0 | 9.1 | 9.7 | 11.2 | 7.2 | 7.4 |
| | 9.5 | 9.3 | 5.8 | 4.3 | 8.2 | 6.7 |
| | 18.0 | 9.4 | 15.0 | 6.9 | 15.6 | 6.4 |
| MEANS..... | 11.5 | 8.9 | 9.6 | 6.6 | 11.4 | 6.0 |

erythroid aplasia of the bone marrow and benign thymoma,¹ and, more recently, an intensified interest in thymoma and its role in relation to the lymphoid system and the immune response.¹

A causal relationship between benign thymoma and erythroid aplasia of the bone marrow has not been clearly demonstrated. However, it has been suggested that the thymoma may produce a humoral factor or antibody which inhibits erythropoiesis, perhaps by affecting erythropoietin. Jepson and Lowenstein (1966)³ demonstrated "an erythropoietic inhibitor . . . in the plasma of each of two patients with erythroblastopenia." One of these patients had a thymoma, the removal of which did not result in remission of the anemia. Plasma from the patient with thymoma and red cell aplasia inhibited the erythropoietic response of polycythemic mice to exogenous human erythropoietic stimulating factor as determined by 48-hour ⁵⁹Fe incorporation into erythrocytes.

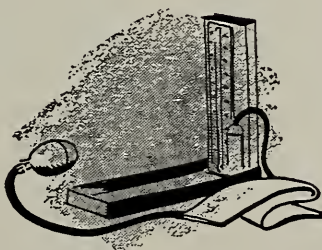
The data presented in this paper suggest that

serum from a patient with benign thymoma and erythroid aplasia caused a partial suppression of erythropoiesis in weanling rats when injected intravenously for five days, as measured by reticulocyte counts.

These data indicate that further attempts should be made to detect a factor in patients with benign thymoma and erythroid aplasia which may suppress erythropoiesis, in order to clarify the relationship between the thymoma and this interesting and obscure form of anemia.

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CASE REPORTS

"Q" Fever Hepatitis

Report of a Case in the Mojave Desert

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AND JOHN J. VAN DYKE, M.D.,
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THE LITERATURE in recent years has brought to light the numerous diseases of protean manifestation, not the least among which is "Q" fever, that are caused by the rickettsia *Coxiella burnetii*. "Q" fever was originally described as a disease distinct from, but often similar in its manifestations to, typhus fever and leptospirosis. In the past few years the literature, particularly from California, Australia and Canada,¹⁰ has been focusing upon liver involvement in this disease.

The following is a case report of anicteric hepatitis occurring in one of the military personnel at George Air Force Base, Victorville, California, in the upper Mojave Desert. There has never been such a case reported before in this community of 80,000 people in the Victor Valley.

Report of a Case

A 33-year-old staff sergeant, USAF, was well until 9 June 1965, when a fever of 37.2°C (99°F), non-productive cough, sore throat and headache developed. The patient said he had not been out of the state for two years, had been around no one

else with similar symptoms and kept no pets. He had received no injections or transfusions in the preceding 18 months. For two days before visiting the clinic, he had noted "dark yellow, almost brownish" urine. Physical examination in the clinic was within normal limits except for mild, right upper quadrant tenderness. The liver was not palpably enlarged. Urinalysis was essentially normal and the urine was yellow. Laboratory studies were ordered and the patient was treated with expectorants for a probable viral infection of the upper respiratory tract.

The patient returned in four days, feeling better, although cough, sore throat, and headache still remained. He was afebrile. On physical examination no changes were noted.

The patient returned 17 June, stating that his headache had subsided. He then said that he had begun to have a distaste for cigarettes. With the laboratory studies received (Table 1), it was felt that the patient had anicteric hepatitis, probably viral. This concept changed with the results of the complement fixation studies for "Q" fever, which were diagnostic.

The patient was admitted for liver biopsy on 21 June. At this time he was asymptomatic. An x-ray film of the chest showed no abnormality. A liver biopsy specimen was sent to March AFB, California, where the interpretation was: "There are variations of liver cells as to their nuclear size. The liver cells contain increased amounts of hemisiderin and bile. Occasional polymorphonuclear cells are present in the sinusoids." The pathologist stated the findings were consistent with hepatitis. It should be noted bile was never found in the urine. Since discharge the patient has remained asymptomatic.

Comment

The case was one of anicteric hepatitis caused by "Q" fever. There was no evidence of pneumonitis. How the patient contracted the disease still remains obscure. He had no involvement with horses, sheep

From the 831st Tactical Hospital, George Air Force Base, Victorville.

Submitted 10 October 1966, Revised 31 March 1967.

Reprint requests to: 8920 Wilshire Boulevard, Beverly Hills 90211 (Dr. Karns).

TABLE 1.—Laboratory Findings in a Case of "Q" Fever Hepatitis

| | 10 June | 14 June | 17 June | 21 June | 7 July | 21 July | 16 Sep. | 5 Oct. |
|----------------------------------------------------------------|------------|------------|------------|------------|-----------|------------|--------------|-----------|
| Leukocytes (per cu mm)..... | 6,500 | 6,700 | | | | | | |
| Segmented | 75% | 67% | | | | | | |
| Bands | | } 2% | | | | | | |
| Eosinophiles | | | | | | | | |
| Basophiles | | | | | | | | |
| Atypical | | 10% | | | | | | |
| Lymphocytes | 25% | 28% | | | | | | |
| Monocytes | | 3% | | | | | | |
| Hematocrit | 41% | 39% | | | | | | |
| Sedimentation rate (mm/hr)..... | 18 | 24 | | | | | | |
| Bromsulphthalein | | | | | | | 1% (45 min.) | |
| Serum glutamic oxaloacetic transaminase (Babson units)..... | 64 | 34 | 84 | | 14 | 14 | 15 | |
| Serum glutamic pyruvic transaminase.... | | 126 | 126 | | 18 | | 0 | |
| Alkaline phosphatase (Bodansky units)... | | 3 | 6 | | 4 | 4 | 4 | |
| Bilirubin (mg per 100 ml): | | | | | | | | |
| Total | | | 0.5 | | 0.5 | 0.3 | 0.4 | |
| Direct | | | 0.2 | | 0.05 | 0.1 | 0.3 | |
| Heterophile agglutination | | neg. | | | | | | |
| Cold agglutinins | | | neg. | | | | | |
| Febrile agglutinins | | | | norm. | | | | |
| Lupus erythematosus preparation..... | | | neg. | | | | | |
| Complement fixation for "Q" fever*..... | | | | 1:160 | 1:80 | | | 1:10 |
| Albumin:Globulin ratio | | | | | 3.4:4.0 | 4.4:2.6 | 4.6:3.0 | |
| Thymol turbidity (units)..... | | | | | | 8 | 6.3 | |
| Throat culture | | | | | | neg. | | |

*Done at Sixth Army Laboratory, Fort Baker, California.

or cattle. His only household pet was a dog which had died in March 1965 from "heart worms." He had been at George AFB, Victorville, for two years and had not left the local area in that time.

Complement fixation studies on his wife and children for "Q" fever were negative. There have been no reported cases in humans or animals in this area of the Victor Valley.

There is real possibility that there was transient hyperbilirubinemia and biliuria at the onset of what subsequent studies suggested was an anicteric form of hepatitis. However, the patient was never noted to be jaundiced by his friends or family and no previous blood studies had been done.

Originally "Q" fever was thought of as a condition in which the patient had a high fever, sometimes relapsing in nature, occurring acutely, accompanied by severe cephalgia, a slow pulse rate and no other obvious localizing symptoms. Derrick⁵ said that "Q" fever is to be distinguished from influenza by the mildness or absence in the former of localized respiratory symptoms, . . . by the comparatively slow pulse rate and by the sporadic distribution." Subsequent to this, however, it was realized that the respiratory complaints and find-

ings typical of pneumonia were relatively common in "Q" fever.¹

In a review of cases in California, Clark and co-workers⁴ noted that hepatomegaly and liver tenderness were surprisingly common, occurring in 11 per cent and 7 per cent respectively in a series of 180 cases. However, the occurrence of hepatitis³ and especially anicteric hepatitis¹² as the only manifestation of the disease has been realized more frequently only recently.

Symptomatologically, "Q" fever is characterized primarily by a severe generalized headache. Conjunctival injection is frequently seen; however, only about 10 per cent of patients have a diffuse macular rash. Fever, malaise, anorexia, cough and pleuritic pain are fairly common symptoms. Nuchal rigidity, abdominal pain, vomiting, diarrhea and scrotal pain sometimes occur, but not often.¹

Physical findings are often scant. Conjunctival injection may be seen, as well as pleural friction rubs and rales when there is pulmonary involvement. Scleral icterus, hepatomegaly and liver tenderness are present in 10 to 15 per cent of cases. In some surveys the incidence of splenomegaly was 5 per cent.⁴ Abdominal tenderness and nuchal

rigidity are unusual. Other unusual findings are cardiac murmur, reflex changes, apathy and confusion and scrotal swelling and tenderness.

There have been many descriptions of the pathological changes that occur in this disease, most interest centering around the liver biopsy. Geistl³ described numerous focal lesions with involved liver cells showing an intense acidophilic vacuolated cytoplasm. However, the acidophilic hyaline bodies seen in acute viral hepatitis were not seen. No vascular lesions were seen and Kupfer-Stern cells were prominent. There was an infiltrate of round cells with eosinophils and an occasional polymorphonuclear leukocyte. No giant or epithelioid cells were found. Geistl said: "The lack of fibroblasts and the scarcity of inflammatory cells set [the lesions] apart from true granulomas."¹⁰

Picchi and Nelson reported three cases from the Oakland, California area in which the characteristic pathologic feature of liver biopsy was multinucleated giant cells giving a diffuse granulomatous appearance. They suggested that "Q" fever be considered subsequently in the differential diagnosis of diffuse granulomatous diseases.⁸

Edmundson³ noted the granulomatous changes in the liver and in addition he suggested a sequence of changes characterizing "Q" fever hepatitis as follows: Kupfer cell infection and proliferation gives rise to multinucleated cells; next the sinusoidal wall fragments and swells and this is followed by an infiltrate of neutrophils, round cells and a few eosinophils. Parenchymal cells may or may not undergo necrosis before healing occurs. Characteristic eosinophilic changes in the vascular walls were described. Edmundson also commented on hepatic fundal changes that were stated to be suggestive of "Q" fever.

The differential diagnosis when "Q" fever is considered is becoming longer with every new report. Already it includes infectious hepatitis, infectious mononucleosis, primary atypical pneumonia, typhoid fever, typhus fever, leptospirosis, undulant fever,⁹ acute anemia⁴ and diffuse granulomatous diseases.^{8,12}

Laboratory findings are not unique. Hypocholesterolemia, false positive Kolmer reactions and normochromic normocytic anemia have been mentioned.^{4,11,12} The diagnosis is made serologically. A complement fixation titer of greater than 1:16 is

considered diagnostic by Babudieri.² Clark and co-workers⁴ listed in their criteria a titer of 1:32 or greater as significant.

The prognosis is usually excellent. Patients with hepatic involvement, however, usually have greater morbidity; fatal cases have been reported.³

The need to establish *Coxiella burnetii* as the etiologic agent is important for in many cases there is good response to broad-spectrum antibiotics. Chloramphenicol has been found to be the most effective.^{8,12}

Summary

A case has been presented of a 33-year-old serviceman with "Q" fever presenting as anicteric hepatitis. A brief review of the clinical and pathological findings is presented.

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Pancreatic Pseudocysts In Children

Report of a Case and Review of the Literature

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PSEUDOCYSTS OF THE PANCREAS are not common in childhood. In the world literature fewer than 70 cases have been reported, most of them within the past four years, probably due to increased awareness of the problem. The following case report of a pseudocyst of the pancreas in a seven-year-old child perhaps typifies the clinical evolution of the cyst and the treatment.

Report of a Case

A seven-year-old girl received a severe blow to the epigastrium on 5 November 1966 when, in falling from a bicycle, she was struck by the handlebars. Because of abdominal pain and nausea she was seen by her physician later that day but had improved by the time of the examination and was sent home. There the abdominal pain increased and the patient was admitted to the hospital 8 November 1966.

On admission the hematocrit was 38, leukocytes numbered 13,350 per cu mm and the serum amylase was 1,030 Somogyi units. The working diagnosis was traumatic pancreatitis, with a note to "rule out other intra-abdominal injury."

Fluids and penicillin and chloramphenicol were administered intravenously and an anticholinergic agent, propantheline, was given intramuscularly. The patient received no food or fluids by mouth. She gradually improved and the hematocrit remained stable.

After four days oral feedings were resumed. When she ate meat and protein, however, serum

amylase rose again and nausea returned. She was febrile, temperature rising intermittently to 39.2°C (102.5°F).

Fullness in the left upper quadrant first noted one week after admission gradually became more palpable as a definite mass. On 18 November upper gastrointestinal roentgen studies showed a mass in the area of the pancreas displacing the stomach to the left and to an anterior position.

The clinical impression was now pseudocyst of the pancreas and when the mass enlarged over the next four days, operation was decided upon. The abdomen was opened with a subcostal incision. A large, smooth, fluctuant mass about 12 cm in diameter was palpable behind the stomach in the region of the body of the pancreas. Transgastric cystogastrostomy was carried out. Through an anterior opening in the gastric wall the posterior wall was incised and the cystic mass was opened. More than 500 ml of clear pancreatic fluid was obtained. The amylase content of the fluid was over 80,000 units. The cystogastrostomy opening was secured by a circumferential running suture of 3-0 chromic, a Penrose drain was placed in the left upper quadrant and the stomach and abdominal wall were then closed.

The postoperative course was excellent. Intravenous fluids and nasogastric suction were maintained for five days, then oral feedings were gradually given. No fluid drained from the Penrose tube and it was removed in five days. The child was discharged from the hospital 4 December 1966.

TABLE 1.—Serum Enzymes

| Date | Serum Amylase Somogyi Units (Normal = 60-160) | Serum Lipase Sigma Units (Normal = 0-1) |
|---------------|-----------------------------------------------------|-----------------------------------------------|
| November 1966 | | |
| 8 | 1,030 | 3.8 |
| 9 | 684 | ... |
| 10 | 500 | ... |
| 11 | 450 | ... |
| 14 | 562 | ... |
| 16 | 1,028 | 4.4 |
| 19 | 720 | ... |
| 22 | 900 | ... |
| 23 | 1,200 | ... |
| 24 Operation | ... | ... |
| 26 | 400 | ... |
| 28 | 327 | ... |
| 30 | 500 | ... |
| December 1966 | | |
| 3 | 600 | ... |
| 8 | 600 | 1.1 |
| 15 | 275 | 0.3 |
| 29 | 140 | 0.48 |
| January 1967 | | |
| 25 | 86 | 0.0 |

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Serum amylase gradually declined to normal (Table 1). The abdominal wound healed well and the mass was no longer palpable. The patient now eats all foods and is asymptomatic. She has gained over ten pounds since the operation.

Etiology

Although a history of acute pancreatitis would be significant, trauma is the most common cause of pancreatic pseudocysts in children.^{2,3,7} Following blunt trauma some portion of the ductal system of the pancreas ruptures, bringing about peritonitis that is limited to the lesser omental bursa. The gradual accumulation of pancreatic fluid is confined by the surrounding viscera. As the resulting cyst has no true endothelial lining, it is classified as a pseudocyst.

It is interesting to note that in 11 of the reported cases,^{3,4,8-10,14} including the present one, blunt trauma was due to impact with bicycle handlebars.

Diagnosis

A pseudocyst of the pancreas should be suspected in a child with epigastric pain, and abdominal mass and fever, vomiting and elevation of serum amylase. A history of blunt abdominal trauma or acute pancreatitis is significant. Upper gastrointestinal roentgen studies typically show anterior displacement of the stomach consistent with a mass in the lesser sac.

Renal cysts, gastrointestinal reduplications, mesenteric cysts, teratomas and dermoid cysts, hydronephrotic cysts, a Wilms tumor, neuroblastoma, polycystic kidney and retroperitoneal hematomas should be considered in the differential diagnosis.⁷

Treatment and Comments

When a child is examined immediately following blunt trauma to the epigastric area and there is evidence of peritoneal irritation and the serum amylase content is high, the diagnosis of traumatic pancreatitis is usually made. If injuries to other viscera — such as rupture of the spleen or hollow viscus — can be ruled out, a decision must be made between exploratory laparotomy or continued observation of the patient.

A more aggressive approach to the surgical treatment of traumatic pancreatitis is evident in the current literature.^{11,12} Various surgical procedures have been used including external drainage, resection,

repairing fragmented segments or repairing a divided duct and internal drainage. The early surgical treatment must be fitted to the circumstances.

Once time has elapsed, however, and the patient has not been operated upon and a pseudocyst forms, operation is usually mandatory. Warren¹² mentioned marsupialization, external drainage, excision, resection and internal drainage. Marsupialization is not generally advocated today because of resulting pancreatic fistulas and skin erosion. Although this may also be true for external drainage Bettex¹ expressed the opinion that external drainage is the treatment of choice.

Warren¹³ favored excision over other methods. However the nature of a pseudocyst may make complete excision impossible. Resecting the pseudocyst along with a corresponding portion of normal pancreas entails greater hazard to the patient, in that the spleen usually must be removed; or, in the case of a cyst in the head of the pancreas, pancreaticoduodenal resection becomes necessary.

Internal drainage is currently regarded as the most practical surgical approach.^{2,3,5,7} This is done usually with a Roux-en-Y loop or by anastomosis of the cyst to the stomach. The simplicity of performing a transgastric cystogastrostomy makes this procedure preferable. Post-operative x-ray studies have revealed no barium reflux within twelve weeks of the operation.⁶

Summary

A case of a pancreatic pseudocyst in a seven-year-old child is reported. Treatment via a transgastric cystogastrostomy was very effective and postoperatively the child became asymptomatic.

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Successful Surgical Treatment of Massive Pulmonary Embolization

Report of a Case and Review of the Literature

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ALTHOUGH TRENDELENBURG first described his procedure for pulmonary embolectomy in 1908,¹⁸ the first successful Trendelenburg procedure was not reported until 1924.¹² Up to 1961, only 23 successful Trendelenburg procedures had been reported in the world's literature⁵ and in most centers the results were disappointing.¹⁶

The first successful pulmonary embolectomy performed with the aid of cardio-pulmonary bypass was reported by Cooley and Beall in 1961,⁶ although Sharp¹⁴ apparently performed the first successful procedure but did not report it until one year later. Up to 1965, there had been over 30 case reports of successful pulmonary embolectomy using cardio-pulmonary by-pass.¹³

There are an estimated 47,000 deaths annually from pulmonary embolization in the United States.⁷ In a review of autopsy findings when presumably healthy persons died suddenly, 26 cases of massive

pulmonary embolization were found, five of them in women who died in the first trimester of pregnancy.⁴ The purpose of this paper is to present a report of a case and to review the pertinent principles in the management of patients.

Report of a Case

A 27-year-old white woman was admitted to St. Mary's Long Beach Hospital on 18 November 1966. Seven days earlier, a cesarean hysterectomy had been performed at another hospital, and "large varicose veins" were noted on the right ovary and fallopian tube. The patient was discharged from the hospital, completely asymptomatic, three days before the present admission. About 24 hours before admission she complained of mild shortness of breath, dizziness and lightheadedness. She did not have cough or hemoptysis. Approximately nine hours before admission she became acutely short of breath and complained of left precordial pain radiating to the left side of the neck. Later she noticed pain in the right side of the neck and right shoulder which was related to respiration. She had had no antecedent abdominal pain or swelling of the legs. The past history was completely negative for cardio-respiratory or peripheral vascular disease.

The patient was acutely ill, dyspneic, pale and cyanotic, but cheerful and alert. The pulse rate was 140, and the blood pressure 90/60 mm of mercury. The second heart sound was loudest at the second left intercostal space. There was no right ventricular lift.

An x-ray film of the chest showed enlargement of a pulmonary artery segment of the cardiac silhouette. The descending right pulmonary artery was prominent. No abnormal parenchymal or pleural densities were noted. An electrocardiogram revealed a vertical heart at $+90^\circ$, with inverted T waves in leads V_1 and V_2 . Hemoglobin was 10.7 gms per 100 ml of blood. Leukocytes numbered 12,200 per cu mm. Results of urinalysis were within normal limits.

Intravenous administration of heparin was begun, and approximately two hours following admission a metaraminol drip was started to maintain the blood pressure. The patient continued cyanotic despite constant administration of oxygen. A macroaggregated albumin-iodine¹³¹ lung scan (Figure 1) showed diminished radioisotope distribution in the right middle and lower lung fields. Multiple areas of decreased activity were also detected on the left, indicating a bilateral perfusion deficit. A

Submitted 18 May 1967.

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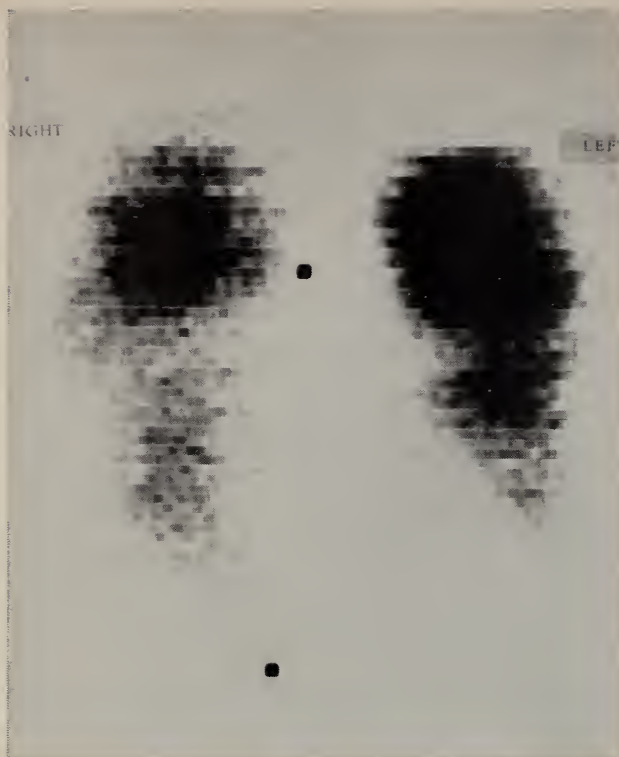


Figure 1.—Lung scan demonstrating extensive bilateral perfusion deficit.

pulmonary angiogram (Figure 2) confirmed the presence of bilateral thrombo-embolic disease. A large concave filling defect was noted at the bifurcation of the right main pulmonary artery. Obstruction was also seen at the level of the distal left main pulmonary artery. Intra-luminal thrombi were noted extending into the lobar pulmonary arterial branches bilaterally. The right ventricular pressure was 40/20 mm of mercury.

On the night of admission, with the patient under local anesthesia, venous and arterial monitoring catheters were established, the right femoral artery and vein were isolated and partial cardiopulmonary by-pass was begun with use of a disposable Travenol bag.* Her color and vital signs immediately improved. General anesthesia was then induced and a median sternotomy incision was made. After total by-pass was established, venous return suddenly diminished. A large thrombus was found occluding the inferior vena cava cannula. After its removal and the reestablishment of adequate venous return, the main pulmonary artery was opened longitudinally and the thrombi pictured in Figure 3 were removed. The pericardium was closed loosely. Simultaneous with the thrombectomy, a clip was placed on the inferior



Figure 2.—Pulmonary angiography demonstrating severe bilateral pulmonary artery obstruction.

vena cava and both ovarian veins were ligated.

The patient did well postoperatively and was maintained with heparin. An x-ray film of the chest showed striking reduction in the size of the pulmonary artery segment and some reduction of the right pulmonary artery.

On 28 November the patient again complained of intermittent chest pain and dyspnea. An inferior venacavagram revealed a functioning and patent plication. A typical appearing configuration³ was seen at the plication site. There was no evidence of trapped thrombus, occlusion or breakdown of the plication. She continued to do poorly in spite of anticoagulation. On 5 December, chest radiography revealed the interval development of an abnormal retrocardiac density compatible with left lower lobe consolidation. Blunting of the right costophrenic sulcus was seen. The cardiac silhouette had enlarged considerably. Significant pulsus paradoxus and diminished heart tones were noted clinically. Pulmonary and right atrial angiography was performed. The films were interpreted as showing delayed opacification and delayed flow to the left lower lobe (Figure 4), and a definite pericardial effusion.

The previous operative site was reopened and a large accumulation of sanguinous pericardial effusion was evacuated. Vital signs immediately

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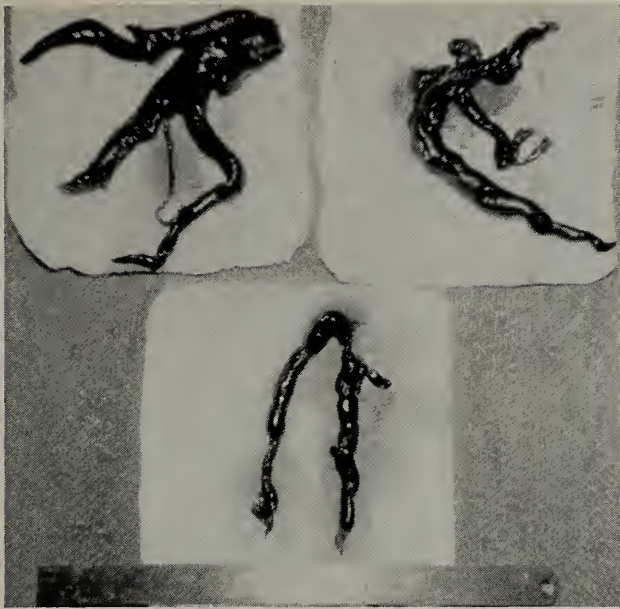


Figure 3.—Thrombi removed from right (top left) and left (top right and bottom) pulmonary arteries.

improved. After considerable debate, exploration of the left pulmonary artery was decided upon in view of the preoperative angiogram, and cardio-pulmonary by-pass was effected. No thrombi were found, however. The left lower lobe of the lung was described as "stiff and discolored." The patient had an uneventful recovery, and was discharged 17 December. When she was last seen, 18 April 1967, an x-ray film of the chest and an electrocardiogram were within normal limits and she was completely asymptomatic.

Discussion

It has been stated that any patient with acute cor pulmonale, shock and cyanosis, secondary to pulmonary embolization persisting for one to two hours, will die without surgical intervention.¹³ Sautter and coworkers¹⁵ have reported two cases in which patients with massive pulmonary embolization without clinical shock survived without surgical intervention. Both of these patients subsequently had normal pulmonary arteriograms. Fred and Axelrad⁹ demonstrated angiographic clearing in seven patients with emboli restricted to lobar and segmental branches. Again, none of these patients was in clinical shock. Houk and coworkers,¹¹ on the other hand, reported a well studied case of chronic pulmonary hypertension with elevated pulmonary vascular resistance and arterial desaturation subsequent to massive pulmonary thromboemboli. The patient was improved by pulmonary thrombectomy approximately five months after the



Figure 4.—Postoperative pulmonary arteriogram demonstrating delayed flow to the left lower and upper lobes.

acute embolic episode. The factors which activate lysis of pulmonary thromboemboli in some patients but not in others are not apparent. It seems, however, that patients with acute massive pulmonary embolization and clinical manifestations of shock, prolonged cyanosis or impairment of vital centers, will not survive long enough for these presumably fibrinolytic factors to operate.

The importance of establishing partial by-pass under local anesthesia before inducing general anesthesia has been emphasized by several investigators.^{1,2,8,13} Ligating the pulmonary artery of dogs, Beall and coworkers¹ found that all animals died within 15 minutes of the induction of general anesthesia, whereas all animals placed on partial by-pass initially, survived for at least one hour.

In the present case the first pulmonary angiogram correlated exactly with the condition observed at operation. The chest roentgenogram at the time of admission, although abnormal, did not reflect the catastrophic intrathoracic condition that was present. There was good correlation with the initial lung scan. However, a lung scan cannot be relied upon as the only diagnostic procedure in thrombo-embolic disease.¹⁰ Pulmonary arteriography is mandatory if pulmonary arterial operation is contemplated.¹⁹ If necessary, cardio-pulmonary by-pass should be established before angiography.

The conditions observed in the second angiographic study in the present case were undoubtedly due to infarction of the left lower lobe from the previous embolization. Asymmetrical filling or prolongation of the arterial phase or "oligemia" is not adequate radiographic evidence of pulmonary embolization if the lungs are otherwise abnormal.¹⁷

Summary

A case of massive pulmonary embolization and successful treatment under cardio-pulmonary bypass is presented. Patients presenting with the clinical picture of massive pulmonary embolization, shock and cyanosis, should be considered for emergency embolectomy following appropriate diagnostic studies. Establishing partial by-pass under local anesthesia before inducing general anesthesia is important to the success of pulmonary embolectomy.

ACKNOWLEDGMENTS. We are indebted to Mr. Thomas King, R.T., for preparing the illustrations for this manuscript. M. W. McCallum, M.D., referred the patient and provided details of the initial operation. Phillip Rothchild, M.D., performed the inferior vena caval plication.

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"Red Eye" as the Presenting Sign of Syphilis d'Emblée

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IN RARE CASES the manifestations of syphilis still challenge the physician's diagnostic skill. Following is a case in which the disease occurred without chancre (syphilis d'émblée) and the initial complaint was referable to the eye. Minimal signs of secondary syphilis, not noticed by the patient, aided in establishing the diagnosis.

Report of a Case

A 25-year-old man sought help from the emergency service of the University of California Medical Center, San Francisco, on 5 August 1964 because of acute "red eye" associated with aching and photophobia for two days. Ocular examination showed chemosis, miosis, conjunctivitis and vascular engorgement of the ciliary vessels of the left eye. Both pupils reacted to light and convergence was normal. The use of compresses and instillation of an ophthalmic solution of sulfisoxazole (Gantrisin®) were prescribed. The patient was referred to the Eye Clinic, where slit-lamp examination showed fine white granular keratinous precipitates, 3+ flare, 3+ cells, and annular posterior synechiae. No inflammation of the choroid or retina was present. The patient was instructed to use ophthalmic solutions of cyclopentolate (Cy-

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Aided by Training Grant TI AM 5372-04 from the United States Public Health Service.

Submitted 26 May 1967.

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clogyl®), phenylephrine (Neosynephrine®) and dexamethasone (Decadron®).

Because of headache, cough, drenching night sweats, intermittent diarrhea and loss of a few pounds of weight, the patient was referred to the Medical Clinic six weeks later. He denied having had gonorrhea or genital lesions, and he had not received antibiotics for many months. A routine serologic test for syphilis in May 1964 (when he was discharged from the Armed Services) had been nonreactive.

On physical examination, the temperature, blood pressure and pulse rate were within normal limits. A few ham-colored papules were noted on the trunk, scalp and extremities. The oral mucous membranes and perianal skin appeared normal. The left testicle was tender on palpation. A soft, nontender jugulodigastric lymph node, 2 cm in diameter, was palpable. The urethra was not indurated.

The packed red cell volume of the blood was

42 per cent. The leukocyte count was 7,050 per cu mm, with a normal differential. The urine was normal. Tuberculin (purified protein derivative) and fungal skin tests and a toxoplasma test gave negative results. A roentgenogram of the chest showed linear densities in the apex of the left lung. Darkfield examination of serum from two cutaneous lesions was negative for *Treponema pallidum*. Biopsy of a cutaneous lesion showed a dense inflammatory infiltrate, containing numerous plasma cells (Figure 1). On 11 September, a Venereal Disease Research Laboratory (VDRL) slide test for syphilis was reactive at a dilution of 1:64. On 21 September, a second VDRL slide test was reactive at a dilution of 1:256, and a diagnosis of secondary syphilis was made. Epidemiologic investigation of sexual contacts was provided by the local Public Health Service facilities.

The patient was treated with 6 million units of penicillin in divided doses over a 15-day period. Chills, fever, malaise and headache developed a few hours after the initial injection but not after subsequent injections. During the next 18 months serologic tests showed a progressive decrease in titer, and the ocular lesions slowly resolved. No further treatment was required after September 1965. A serologic test in April 1966 gave a negative reaction.

Discussion

Of 3,244 patients with early syphilis studied by a cooperative clinical group, 90 had ocular complications, which in 73.3 per cent of cases consisted of iritis or uveitis.¹ In their encyclopedic treatise on the disease in 1944, Stokes, Beerman and Ingraham² stated that syphilis is the causative factor in 30 to 40 per cent of cases of uveitis, that uveitis rarely occurs before the sixth month of infection, and that it is more common in relapsing or recurrent forms of syphilis. The advent of specific therapy for this infection in the quarter century since these statements were made apparently has aided in preventing the occurrence of such ocular complications. In a recent survey of 432 cases of uveitis, only 4.6 per cent were attributed to syphilis.³

Acquired syphilis without chancre is uncommon. Traumatic or needle-prick inoculation is rare, and in most cases the primary lesions are minor or inapparent or occur in hidden sites. Because saphrophytic spirochetes resembling *T. pallidum* are pres-

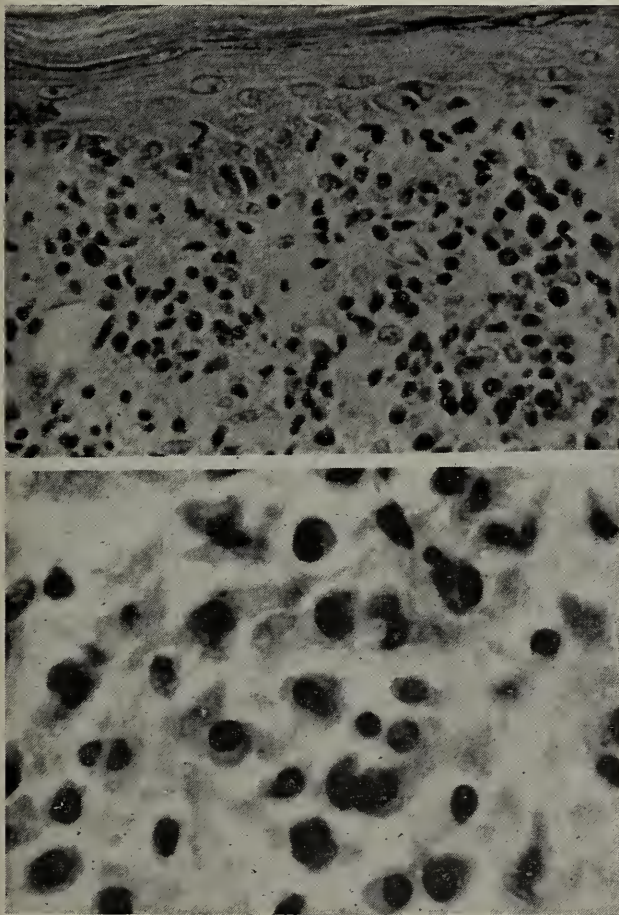


Figure 1.—A. Biopsy specimen of cutaneous lesion, showing dense inflammatory infiltrate composed of mononuclear cells and some histiocytes throughout the dermis. (Hematoxylin and eosin, $\times 400$.) B. Same section at higher magnification, showing predominance of plasma cells in the inflammatory infiltrate, $\times 1,000$.

ent normally in the oral and rectal mucosa, darkfield examination is usually unreliable in screening suspicious lesions in these areas. In such cases the presence of enlarged painless cervical or inguinal lymph nodes may be the only evidence of inoculation.

The patient described in this report had syphilis of less than three months' duration, which occurred with inapparent or no primary lesions. The occurrence of "red eye" due to uveitis as the initial manifestation of the disease is as unusual today as it must have been in the time of the classic syphilographers.

GENERIC AND TRADE NAMES OF DRUGS

Sulfisoxazole—*Gantrisin*.®
Cyclopentolate—*Cyclogyl*.®
Phenylephrine—*Neosynephrine*.®
Dexamethasone—*Decadron*.®

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MEDICAL STAFF CONFERENCE

Occult Malabsorption Simulating Pernicious Anemia

These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California Medical Center, San Francisco. Taken from transcriptions, they are prepared by Drs. Martin J. Cline and Hibbard E. Williams, Assistant Professors of Medicine, under the direction of Dr. Lloyd H. Smith, Jr., Professor of Medicine and Chairman of the Department of Medicine.

DR. BREEDEN*: The patient, a 72-year-old retired carpenter, was admitted to hospital because of shortness of breath on exertion. The patient had been in excellent health until six weeks before admission, when he noted shortness of breath after walking for several blocks. The severity of this symptom increased gradually to the point of shortness of breath at rest or walking about a room. In addition he had noted several episodes of watery stools during the immediate six-week period.

The patient appeared confused and chronically ill, and he had respiratory distress at rest. Blood pressure was 195/115 mm of mercury, the pulse rate 82 per minute and irregular, respirations 30 per minute and temperature 37°C (98.6°F). The skin was pale and slightly yellow. Neck veins were flat with the patient upright. Decreased breath sounds, dullness and fine rales were noted at both lung bases. The heart was enlarged to the anterior axillary line; no gallop or murmur was heard. Examination of the abdomen was within normal limits. Pitting edema was present over both ankles. Neurological examination demonstrated decreased vibratory and position sense in both feet. Both ankle jerks were absent.

Laboratory data: hematocrit, 18 per cent, leukocytes 2,000 per cu mm with 33 per cent polymorphonuclear cells, 4 per cent eosinophils, 53 per cent lymphocytes and 10 per cent monocytes. Many of the polymorphonuclear leukocytes had an increased number of lobes in the nucleus.

There were 178 nucleated red blood cells per 100 leukocytes. The red cells appeared to be macrocytic. The platelet count was 58,000 per cu mm, with reticulocytes 0.6 per cent. Serum electrolytes were within normal limits. Serum proteins were 5.0 gm per 100 ml (2.8 gm albumin) and serum carotene 0.004 mg per 100 ml (normal 0.05 to 0.30 mg). Seventy-two hours fecal fat excretion was 1 per cent (normal less than 5 per cent); D-xylose excretion in five hours 9 per cent (normal more than 20 per cent); gastric analysis for free acid, negative; no acid after histamine stimulation; Schilling test without intrinsic factor, 3 per cent; with intrinsic factor, 1 per cent. A bone marrow examination revealed many megablasts. X-ray examination of the small bowel demonstrated delayed transit time, generalized dilatation, but no evidence of segmentation or flocculation. Attempts to obtain jejunal tissue for biopsy were unsuccessful.

The patient was believed to have malabsorption syndrome. After treatment with parenteral vitamin B₁₂, reticulocytosis occurred and a rise in the hematocrit level followed. Treatment with digitalis and mercurial diuretics was followed by diuresis and improvement in dyspnea and weakness. At discharge from the hospital the patient was taking vitamin B₁₂, folic acid and a gluten-free diet.

DR. WUEPPER*¹: During the past two years, I

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*¹Kirk D. Wuepper, M.D., Research Fellow in Dermatology and Immunology.

have been involved in a study of patients and their relatives with proved or suspected immunologic diseases. We have been establishing tests for serum antibodies of the type found in certain thyroid diseases, pernicious anemia, idiopathic adrenal insufficiency and a growing list of diseases believed to occur on an immunologic basis. If we are to give credence to a positive serologic test of this sort, and if the test is to become a useful diagnostic laboratory measurement, these antibodies should be found regularly in cases of the disease. Furthermore, false-negative tests must be explained. That is, the tests must be both sensitive and specific.

The case of the patient presented this morning is instructive, not because of positive results of immunologic tests but because they were absent. The association of gastric parietal cell antibodies with pernicious anemia is so constant a feature that failure to demonstrate the antibody should lead to reevaluation of the evidence upon which the diagnosis was made. Initially this patient was considered to have addisonian pernicious anemia. To support this were the findings of megaloblastic erythropoiesis in the marrow, gastric achlorhydria, decreased absorption of radiolabeled vitamin B₁₂ and the neurologic expressions of the disease—mental cloudiness and posterior column degeneration. A serum specimen was negative for gastric antibodies. The hematologic findings were those of megaloblastic anemia; the neutrophilic polymorphonuclear leukocytes were hypersegmented, the leukocyte count and platelet count were decreased, the mean cell volume and mean cell hemoglobin were increased but the mean cell hemoglobin concentration was normal; and the reticulocyte count was normal. The circulatory findings could be explained by the anemia; the neurologic manifestations suggested that vitamin B₁₂ deficiency was implicated. We therefore turned to the megaloblastic anemias for a solution to the problem. (Table 1)

Megaloblastic anemia is the hematologic expression of an underlying defect in nucleoprotein synthesis. In 95 per cent of patients this defect is corrected by administration of vitamin B₁₂ or folic acid or both. These vitamins serve as co-enzymes in the biologic synthesis of nucleoproteins. Deficiencies in either of these vitamins result from inadequate ingestion, malabsorption or impaired utilization. Once this occurs, tissue stores of folic acid are exhausted in three to six months and

of vitamin B₁₂ in three to six years.

Vitamin B₁₂ deficiency occurs on a nutritional basis mainly in strict vegetarians who eat no animal proteins. Addisonian pernicious anemia results from a decrease or absence of gastric intrinsic factor, which promotes absorption of the large vitamin B₁₂ molecule from the distal small intestine. Gastric atrophy has been shown to be a fundamental and constant accompaniment of pernicious anemia. The gastric mucosa shows disappearance of parietal and chief cells and infiltration of lymphocytes and plasma cells. Acid production is absent and the volume of gastric juice is reduced. Castle, in 1929, demonstrated that it was not gastric acid but a substance present in gastric juice, "intrinsic factor," that facilitated absorption of the extrinsic factor present in the diet. The extrinsic factor we now know to be vitamin B₁₂. Intrinsic factor is a mucoprotein or glycoprotein with a molecular weight of approximately 65,000. Recent evidence suggests the pa-

TABLE 1.—*The Megaloblastic Anemias*

| |
|-----------------------------------------------------------------------------|
| I. Corrected primarily by vitamin B ₁₂ |
| Inadequate ingestion |
| Nutritional deficiency ("vegans") |
| Inadequate absorption |
| Pernicious anemia (decreased or absent intrinsic factor) |
| Surgical resection |
| gastric |
| small intestine |
| Diversion of ingested vitamin |
| <i>Diphyllobothrium latum</i> |
| "blind loop" syndrome |
| Malabsorption syndromes (sprue, idiopathic steatorrhea) |
| Inadequate utilization |
| Antivitamin B ₁₂ agents (no clinical use now) |
| II. Corrected primarily by folic acid |
| Inadequate ingestion |
| Nutritional deficiency |
| Increased requirements |
| megaloblastic anemia of pregnancy |
| megaloblastic anemia of lactation |
| Inadequate absorption |
| Tropical malabsorption syndrome |
| Non-tropical sprue, idiopathic steatorrhea |
| Drug associated |
| anticonvulsants—e.g., primidone (Mysoline®), phenobarbital |
| tuberculostatics—e.g., para-aminosalicylic acid |
| Inadequate utilization |
| Folic acid antagonists—e.g., methotrexate |
| III. Inborn errors of metabolism |
| Defective or absent intrinsic factor synthesis (juvenile pernicious anemia) |
| Selective intestinal malabsorption intrinsic factor-B ₁₂ complex |
| Defective nucleoprotein synthesis |
| Orotic aciduria |
| IV. Cancer chemotherapeutic agents |
| Antipurines |
| Antipyrimidines |

rietal cell is the site of intrinsic factor synthesis.

Inadequate absorption of vitamin B₁₂ occurs also in patients subjected to gastric resection or in patients in whom the absorptive site in the small intestine is diseased or resected—as, for example, in regional enteritis. The vitamin may be diverted from the host and utilized by intestinal microorganisms, in the case of enteroenteric fistulae, or by the fish tapeworm. Impaired utilization of absorbed vitamin B₁₂ is as yet unknown; however, this may be expected if antivitamin B₁₂ agents are introduced for the treatment of cancer.

Folic acid deficiencies may result from nutritional causes or destruction of the vitamin by cooking in large volumes of water. In patients with marginal ingestion of folic acid the additional requirements imposed by pregnancy, lactation or infection may lead to overt deficiency. Inadequate absorption of folic acid occurs in tropical and non-tropical sprue.

In certain patients receiving tuberculostatic or anticonvulsant drugs, a deficiency occurs apparently by competitive inhibition of folic acid absorption. Inadequate utilization may result from administration of folic acid antagonists.

Megaloblastic anemia also occurs as an important sign in certain inborn metabolic defects. This may be due to inherited failure of intrinsic factor production or selective intestinal malabsorption of the intrinsic factor-vitamin B₁₂ complex. Megaloblastic anemia may also result from an inborn error in nucleoprotein synthesis, such as orotic aciduria, or it may arise from the use of antipurine or antipyrimidines in the chemotherapy of cancer.

To return to the patient presented today, inborn metabolic defects and drug-associated causes of anemia can be excluded. His diet, although not above reproach, was not grossly deficient in either vitamin. There had been no operations and the stool was free of intestinal parasites. Additional laboratory evidence made the diagnosis of pernicious anemia unlikely: A Schilling test with added intrinsic factor failed to improve absorption of vitamin B₁₂. Serum levels of both vitamin B₁₂ and folic acid were decreased, and immunoassay of intrinsic factor in the gastric juice was within normal limits.

How is this latter test performed? In 1963, Ardemin and Chanarin described a method for the detection of serum antibodies to intrinsic factor.¹ This method, the charcoal absorption tech-

TABLE 2.—Charcoal Assay of Gastric Intrinsic Factor and Serum Antibodies to Intrinsic Factor

| | |
|------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Principle: | Vitamin B ₁₂ is normally transferred to serum <i>in vitro</i> in the presence of intrinsic factor. |
| Method: | Ardemin and Chanarin ¹ Irvine ⁴ |
| Reagents: | Serum Buffer Gastric juice 57 Co-labeled vitamin B ₁₂ Activated charcoal |
| Test: | After reacting mixture at room temperature for 20 minutes, "unbound" vitamin B ₁₂ is removed by shaking with charcoal. Centrifuge, count supernatant radioactivity. |

nique (Table 2), relies on the principle that vitamin B₁₂ is transferred to serum *in vitro* in the presence of intrinsic factor. Clearly, either serum or gastric juice may be varied in this test. Therefore it is adaptable to (a) determination of serum antibody to intrinsic factor or (b) determination of intrinsic factor itself. This provides a direct assay for the substance lacking in Addisonian pernicious anemia. Irvine demonstrated a sharp delineation of the amount of intrinsic factor present in the gastric juice of patients with pernicious anemia, latent pernicious anemia and normal subjects.⁴ A test measuring gastric intrinsic factor is appealing for several reasons: It can be done quickly, simply and economically; radioactive materials need not be administered systemically to patients; vitamin B₁₂ need not be given in unphysiologic amounts during the period of investigation; and the test can be performed at the time of routine gastric analysis.

As determined by the charcoal absorption method, 60 per cent of patients with pernicious anemia have antibodies to intrinsic factor. Why some patients with pernicious anemia do not have intrinsic factor antibodies is not clear. Some patients have antibodies detectable in the gastric juice and not by serum assay.

The gastric parietal cell antibodies, distinct from intrinsic factor antibodies, are easily determined by the indirect immunofluorescent method.⁶ Control or test sera are exposed to slices of gastric mucosa. These slices are washed and then allowed to react with fluorescein-conjugated antisera. Cytoplasmic fluorescence is positive for the antibodies. Irvine and coworkers⁴ reported over 90 per cent of patients with pernicious anemia had parietal cell antibodies. All patients with proved intrinsic factor deficiency by immunoassay had parietal cell antibodies. This suggests that

the parietal cell antibody test, although a reflection of "autoimmune" gastritis, is a sensitive screening test for pernicious anemia. Patients with positive parietal antibody cell tests should have analysis for gastric acid. If free acid is not detected, a specimen of gastric juice should be submitted for intrinsic factor estimation.

Certain studies suggest that pernicious anemia is a genetically determined disease. Relatives of patients with pernicious anemia have an increased incidence of gastric achlorhydria and gastric carcinoma. When tests of vitamin B₁₂ absorption became available, a significant number of relatives of patients with pernicious anemia were shown to have impaired vitamin B₁₂ absorption. In studies by Callender and Denborough,³ 52 of 308 relatives of patients with pernicious anemia had achlorhydria. Twenty-six of these patients had abnormal absorption of vitamin B₁₂ and in ten of them the absorption was in the range found in pernicious anemia.

When the new immunologic tests were performed on first-degree relatives of patients with pernicious anemia, 35 per cent were shown to have parietal cell antibodies. In one series, 20 asymptomatic first-degree relatives with parietal cell antibodies were studied, and 16 had histologic evidence of gastritis, 11 had achlorhydria, six had impaired B₁₂ malabsorption and one had intrinsic factor antibodies.⁷ In a remarkable family reported by Ardemin and coworkers² six of nine siblings had pernicious anemia and all nine had parietal cell antibodies. These antibodies were present in ten of seventeen offspring of the nine siblings. The results of gastric biopsy showed older members had superficial gastritis.

The patient described this morning did not have pernicious anemia. A malabsorption syndrome best accounts for the combined vitamin B₁₂ and folic acid deficiencies.

Of the megaloblastic anemias, classic Addisonian pernicious anemia should be regarded as a genetically determined disorder of immunologic tolerance. This is manifested by a progressive loss of gastric glands and of intrinsic factor production. This disease is associated with the production of serum antibodies to two cellular constituents of the involved tissue: (1) a cytoplasmic component of the gastric parietal cells, and (2) a product of these cells, intrinsic factor. Until the exact role of these antibodies is delineated, it is impossible to conclude whether the antibodies are

pathogenic or merely concomitants of the disease process. A growing body of evidence suggests that intrinsic factor antibody is able to combine specifically with the intrinsic factor molecule and prevent absorption of the vitamin B₁₂-intrinsic factor complex. Regardless of these considerations, these tests do serve as useful immunologic "markers" because of their close association with impaired intrinsic factor production and gastritis.

DR. SMITH*³: Thank you, Dr. Wuepper. Are there any questions or comments?

PHYSICIAN IN AUDIENCE: Are parietal cell antibodies found in any of the megaloblastic anemias due to folic acid deficiency?

DR. WUEPPER: Parietal cell antibodies are found in about 7 per cent of adults. The incidence is slightly higher in women than men and it increases with age. Clearly, this immunologic abnormality is common and may be found in folic acid deficient patients.

The critical event in Addisonian pernicious anemia is probably the development of antibodies to intrinsic factor. It is doubtful if this occurs in more than one in 50 persons with the parietal cell antibody. Immunoassay for gastric intrinsic factor would be an important determination in such cases.

DR. WILLIAMS*⁴: What are the results of these antibody studies in juvenile pernicious anemia?

DR. WUEPPER: In juvenile pernicious anemia, gastric acid is present and the disease results from failure of intrinsic factor synthesis, a genetically inherited inborn metabolic error. Tests for parietal cell antibodies and antibodies to intrinsic factor are negative in this disease.

PHYSICIAN IN AUDIENCE: Do serum antibodies to tissues other than gastric mucosa appear in pernicious anemia?

DR. WUEPPER: There is a significant association of organ-specific antibodies to thyroid in patients with pernicious anemia. In 1962 Irvine and coworkers⁵ demonstrated antibodies fixing complement with thyroid extract in 15 of 41 patients with pernicious anemia.

Editor's Follow-Up:

After three months of therapy with vitamin

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*⁴Hibbard E. Williams, M.D., Assistant Professor of Medicine.

B₁₂, folic acid and a gluten-free diet the patient was readmitted for study. The hematocrit was 38 per cent and red blood cell indices had returned to normal; 72 hour fecal fat excretion was 5 per cent; serum albumin 4.3 gm per 100 ml; D-xylose excretion 13 per cent (five hours). A Schilling test without intrinsic factor demonstrated 16 per cent excretion in 24 hours.

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EDITORIAL

An Editor's Farewell

TWENTY-ONE AND A HALF years is a long time in the life of a medical journal—it is the whole length of life of CALIFORNIA MEDICINE under this name. The forebears of CALIFORNIA MEDICINE — THE TRANSACTIONS OF THE MEDICAL SOCIETY OF THE STATE OF CALIFORNIA, first published in 1897; THE CALIFORNIA STATE JOURNAL OF MEDICINE, first published in 1902 and CALIFORNIA AND WESTERN MEDICINE, to which the name was changed in 1924 — gave CALIFORNIA MEDICINE a long and well known ancestry when it first appeared in July 1946.

It has been the willing plight of this editor to have served the California Medical Association and this journal continuously since July 1946. This has been a most interesting and stimulating time for the California Medical Association, a period of very rapid growth, of great controversy in medicine and of most significant developments in the science of medicine and of changes in society. From a membership of less than 8,000 in 1946 the Association has grown to over 22,600 active members while the number of medical schools in the state has doubled, to eight, in this period. Since World War II the CMA has come to occupy a position of great importance and leadership in the state of California and the United States. Among

state societies it has become the leader in the socio-economics of medicine, and its role in the legislative process in California, while often difficult, has been the envy of many other state medical associations. The close relationship of the CMA and the medical schools during the recent great changes in the relationship of medicine and society has been at once a tribute to the leaders of the profession and of the medical schools. Among state medical associations at the national level in the American Medical Association, the CMA stands second in numbers but first in influence. For years the California delegation has stood as the leading delegation in the House of Delegates of the AMA. From this delegation in 15 years have come four Presidents of the AMA, three Trustees, one Speaker of the House and a host of chairmen and members of councils and committees.

CALIFORNIA MEDICINE has attempted to reflect some of these great developments over the years but most of all it has attempted to reflect scientific developments in medicine in California. At first a great part of CALIFORNIA MEDICINE was given over to reporting, in monthly installments, what went on at annual sessions of the CMA. In more recent years the journal has turned increasingly to a reflection of trends in the art and science of medicine in the state unrelated to the annual sessions. To some degree it has succeeded in this change in direction. But because of a circulation limited essentially to membership of state associations, state medical journals are not looked upon favorably as a vehicle for publication by those who are advancing the science and art of medicine. The audience is too general, the number of readers of any one kind too small, and commonly the peer

groups of many of the authors with the most sought after material have no interest in reading such journals.

Despite all the efforts of their editors, state medical journals reach a plateau — limited as they are by numbers of subscribers, by the widely varying interests of potential readers and by limited ability in the single state to generate sufficient good scientific material. In fact there are few successful general medical journals. Most journals now cover only a field of special interest.

As regards CALIFORNIA MEDICINE, these limitations must be viewed in light of the fact that scientific medicine in California is growing in strength. This is clearly shown by the eight medical schools of the state and has been recognized by the California Medical Association in its development of the Scientific Board formed to pull together and make effective all the scientific and educational activities of the Association.

CALIFORNIA MEDICINE is no exception to the "rule of the plateau" but its future should be great as it assumes increasingly a role of a regional national medical journal. Already it holds high the need for good editing, for the precise clear statement, for brevity, for accuracy and for a summary that is a summary.

With a total of 14 medical schools in the Western United States, and more to develop, with an outstanding new editor and associate editor closely attuned to organizational and scientific achievement of high degree and in a position to relate closely to the prime source of scientific developments in medical schools, this journal should in the next ten to fifteen years become the leading regional medical journal in this country and eventually a journal of high scientific stature in the United States. The West is young, progressive, growing, and the future here of medicine and of other professions and business is great.

Finally, it has been at once a pleasure and a source of great stimulation and interest for me to have participated in and watched the progress of the CMA in the past twenty-one and a half years and to have reflected some of this progress on the

pages of CALIFORNIA MEDICINE. I am grateful to have had the opportunity and to have had close relationship with all the great leaders in the CMA during this period. They have given me continuing support, lasting friendships and above all, by example, have been my teachers.

I am pleased to acknowledge again that it was John W. Cline who led me into this position by persuading the Council to appoint me Editor. From that time forward many members of the Editorial Board of CALIFORNIA MEDICINE have been most helpful and have given countless hours to the journal. I acknowledge continuing support over the years from the members of the Council and of the House of Delegates of the CMA, from the Committee on CALIFORNIA MEDICINE of the Scientific Board and from the Advisory and Policy Committees of CALIFORNIA MEDICINE. Countless consultants and book reviewers have helped in easing the burden of the Editor. Howard Hassard, John Hunton, Robert Thomas, William Whelan, Mel Tyler and others over the years have been extremely helpful with advice, with editorials and with support. However, most of all I am grateful to Robert F. Edwards, assistant to the editor, who has been my most effective teammate on the journal almost from the first day. It is he who has been responsible for the good editing, the clear statement, the effective summary. And he has done it superbly. Barbara Rooney, as secretary of the Editorial Board and of the journal, has over the years supplied a loyalty and an interest which have made personal and effective the routine as well as the unusual chores of the office.

To all these and to the members of the California Medical Association I am grateful and thankful. To Malcolm Watts and Lloyd H. (Holly) Smith, Jr., who are respectively Editor and Associate Editor, starting with Volume 108, I express my belief that they have the desire and capacity and will have the support to make CALIFORNIA MEDICINE a much better journal — an outstanding journal, of which all of the members of the Association will be proud.

DWIGHT L. WILBUR

California Medical Association



NOTICES AND REPORTS

Council Meeting Minutes

537th Meeting

Tentative Draft: Minutes of the 537th Meeting of the Council, Los Angeles, Airport-Marina Hotel, 30 September 1967.

The meeting was called to order by Chairman Miller at the Airport-Marina Hotel, Los Angeles, on Saturday, 30 September at 10:30 a.m.

A quorum was present and acting (full roll call, including names of invited guests, appears in Item 30).

1. Minutes for Approval

The minutes of the 536th Meeting of the Council, held 26 August 1967, were approved with the following corrections:

| | |
|--------------------------------------------------------------------|------------------------------|
| JOHN G. MORRISON, M.D. | President |
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| 1515 N. Vermont Ave., Los Angeles 90027 • 213 663-8071 | |
| RICHARD W. LEMOS | Sacramento Office |
| 1127 11th St., Sacramento 95814 • 916 444-7496 | |

a. Under item five (CMERF Criteria for Acceptance of Funds), the following sentence was inserted before the last sentence in the first paragraph: "Mr. Hassard stated that as a member of the CMERF Board of Directors, he would certainly want to consider what the ultimate end would be. He suggested that a statement of this kind should be adopted by the CMERF Board and transmitted to the Council."

b. Under item 20, paragraph 5 (pertaining to the CMA staff life insurance program) the last sentence was corrected to read: "Doctor Kay said that the total annual additional premium would be about \$1,000."

c. Under item 21, paragraph 3, the action was amended to conclude with the phraseology: "potential interference in clinical laboratory and other areas of the practice of medicine by a state agency through a mechanism developed under the Medicare program."

2. AMA Activities

AMA Board of Trustees member Burt L. Davis commented on the recent meeting of the World Medical Association in Madrid. One full day of the meeting was devoted to discussion of world population problems. During another session the WMA considered medicine's role in society.

Doctor Davis also reported on a recent meeting of the AMA Board of Trustees, during which board members received valuable speech instruction utilizing video-tape playbacks, under the supervision of a professor of public address. Doctor Davis said that AMA will make this same

service available to state and county medical associations, and suggested that the CMA Council might want to consider participating in such a session.

Doctor Lee Blanchard, newly appointed assistant director of the AMA Department of Undergraduate Medical Education, was introduced by Doctor Davis. Doctor Blanchard, who will also be secretary of the AMA Committee on Family Practice, commented on his new responsibilities.

Mr. Jerry Gould, AMA field representative, briefly reported on some recent developments regarding national health legislation.

3. *Alcoholism*

Chairman Miller read a letter from LACMA President Boyle, concerning a proposal of the LACMA Council that CMA establish a Committee on Alcoholism. After some discussion on the subject, the Council made the following decision:

ACTION: *Voted to request the Chairman of the Council to refer the suggestion to the Committee on Mental Health or other appropriate committee (or the Committee on Committees).*

4. *Volunteer Physicians for Vietnam*

President Morrison read a letter from AMA President Milton Rouse, suggesting that each state medical association should sponsor a given number of physicians annually to serve in caring for victims of the war in Vietnam. Doctor Rouse additionally suggested that medical associations might want to "adopt" a hospital in Vietnam, providing it with necessary staff. It was pointed out that CMA currently has more physician volunteers in Vietnam than any other state—39. It was agreed that Doctor Morrison would write a preliminary response to the letter, waiting until more background information could be made available before requesting Council action on the proposal.

5. *Task Force on 89-749*

President-Elect Malcolm C. Todd, chairman of the CMA Task Force on Public Law 89-749 (Comprehensive Health Planning) reported on the organization and beginning activities of the State Health Planning Council, of which Doctor Todd is an appointed member. He presented for Council consideration, the following proposed statement of the functions of the CMA Task Force on Public Law 89-749:

(1) To examine the relationships between the

California Medical Association, its component and district medical societies, the allied health professions and all segments of the community, to the various levels of government in the implementation of the Comprehensive Health Planning Act;

(2) To provide information, and serve as a stimulus to, the medical profession of the state and its organized units, in the formation of local comprehensive health planning councils, as embodied in P.L. 89-749, for the purpose of:

a. establishing local or area goals and objectives as related to the provision of comprehensive personal and environmental health services;

b. inventorying those local resources and capabilities currently available;

c. determining gaps in the provision of services, or in the existence of facilities or of manpower;

d. establishing those immediate and long-range priorities and goals to overcome any existing deficiencies, and

e. creating mechanisms for the continuing evaluation of performance in attaining short and long-range objectives, as well as in formulating new goals and objectives;

(3) To encourage a "community of involvement" of all interested and concerned professionals and consumers in working toward the planning and program objectives of the Act, and

(4) To preserve, utilize and strengthen the efforts of existing voluntary health planning mechanisms.

ACTION: *Voted to approve the above as functions of the Task Force on Public Law 89-749.*

Doctor Todd also requested that the Task Force be granted a budgetary allocation of \$5,000 to carry out these functions.

ACTION: *Voted to refer the request of \$5,000 for the Task Force on Public Law 89-749 to the Finance Committee.*

6. *Committee on Committees Recommendations*

Chairman Miller, on nominations presented by President-Elect Todd on behalf of the Committee on Committees and the Council concurring, made the following appointments:

Task Force on P.L. 89-749—Marvin Shapiro, M.D., Encino; Gerald Besson, M.D., Sunnyvale; Joseph Telford, M.D., San Diego (replacing three previously appointed physicians who were unable to serve).

Commission on Community Health Services—Marvin Shapiro, M.D., Encino (replacing Harold Kay, M.D.).

Committee on Continuing Medical Education—Richard Opfell, M.D., Santa Ana, as an additional Area Representative (pending approval of the Executive Committee of the Scientific Board).

Committee on Welfare Medical Care Programs—Oscar Powell, Jr., M.D., Oakland, as a consultant.

President-Elect Todd also announced CMA nominations for various councils and committees of the AMA, stating that it was recommended that all California members of AMA committees who are eligible for reappointment be retained in their present positions. The following nominations were announced:

Committee on Occupational Toxicology—Patrick J. Clancy, M.D., Sacramento, to replace Rutherford T. Johnstone, M.D., deceased.

Council on Scientific Assemblies—John C. Wilson, Jr., M.D., Los Angeles County (replacing Walter Scott, M.D., ineligible for re-election).

Committee on Medical Aspects of Sports—Bernard J. Michela, M.D., Long Beach, as an additional member of the committee.

Subcommittee on Hematopoietic and Lymphatic Systems—Paul Hattersley, M.D., Sacramento, as an additional member.

7. *Committee on Legislation*

In the absence of Chairman Dan O. Kilroy, Mr. Ben Read commented on a 24-page, bound booklet reporting on each piece of state legislation of interest to medicine during the 1967 session of the Legislature. The booklet was distributed to the Council and guests for their reference. Chairman Miller thanked the committee for the excellent presentation. Mr. Read also briefly commented on the interim hearings to be held on two major subjects: osteopathy and malpractice insurance.

8. *Drug Abuse*

Speaker William Quinn reported that Assemblyman Duffy's Public Health Committee was pleased to have available to it CMA's recent statement on drug abuse as it conducted hearings on this subject. Doctor Quinn also cited some new evidence of the adverse effects of marijuana.

9. *Commission on Hospital Affairs*

Chairman MacLaggan reported on the 29 August meeting on utilization review, sponsored by the Department of Health, Education and Welfare. He stated that the nature of utilization review and the role of the carrier in it received extensive discussion. Among suggestions for better utilization review were: (a) more involvement of non-physicians (administrators, nurses, social workers, medical record librarians, etc.), (b) more training in techniques of utilization review in medical schools, and (c) priority attention for extended care facilities.

Doctor MacLaggan also reported that the contract for medical staff surveys on a consulting basis with the State Department of Public Health was to be extended. The next group of such surveys, he said, would cover about 60 hospitals, many of which were being resurveyed because they were weak in one or more areas of evaluation. Doctor MacLaggan said that utilization review committees would receive special attention during the coming surveys.

Chairman MacLaggan touched briefly on discussions being carried on with the Subcommittee on Extended Care Facilities regarding the development of definitions to be used in utilization review of patients in extended care facilities. He said that when the definitions had been refined, they would be distributed to the Council.

On behalf of the commission, Doctor MacLaggan recommended that the Council authorize the California Medical Education and Research Foundation to apply for a government grant to explore further the type of patients, the type of care provided, and the cost of obtaining and providing this care in extended care facilities.

ACTION: *Voted to authorize CMERF to proceed in obtaining a government grant for a study of care in extended care facilities (to be conducted in cooperation with the Commission on Hospital Affairs).*

Doctor MacLaggan also suggested that every CMA publication should emphasize as frequently as possible the importance of utilization review.

ACTION: *Voted to request that every CMA publication should carry an item on utilization review as frequently as possible.*

As the final item in his report, Doctor MacLaggan gave the following report on 1967 House of Delegates resolutions referred to the commission:

3-67 Certification and Recertification — Since certification and recertification is being considered

by Congress, the resolved portion of this resolution will not be implemented at this time.

76-67 Admission Procedures to General Hospitals — It was suggested that Doctor Leonard Asher and Doctor Joseph Boyle be contacted regarding the intent of this resolution, i.e., should a study be carried out or should admission committees be suggested.

90-67 Hospital Accreditation Requirements — This resolution has been implemented by referral to the American Medical Association.

108-67 Legislation-Influenced Change in the Practice of Medicine — This resolution has already been implemented through CMA communications and by referral to the AMA.

10. *Tulare County General Hospital Survey*

Councilor Ralph W. Burnett reported on the special survey of Tulare County General Hospital, which CMA had been requested to conduct for the purpose of assessing staffing needs and recommending means by which such needs might be met. Doctor Burnett said that the survey report had been completed and submitted to hospital officials. It was pointed out that reports of this kind were not subject to Council approval.

11. *Bureau of Research and Planning*

In the absence of Chairman Anderson, Councilor Eastman reported that the bureau would be submitting results of two studies to the Council for its approval at the next meeting. One study is on smoking; the other, on the use of proctosigmoidoscopy by California physicians.

12. *California Hospital Association*

Henry X. Jackson, president of the California Hospital Association, discussed the current status of Medi-Cal, stating that his association continues to be committed to the concept of "mainstream" health care for all welfare recipients, with free choice of physician and hospital, reiterating CHA's opposition to the reintroduction of the "corridor" concept. He stated that his association believes the most needed restoration in the program is elective surgery and said he was confident that the Health and Welfare Agency has every intention of restoring all services to the program as soon as fiscally feasible.

Mr. Jackson drew the attention of the Council to the independent actuarial study of Medi-Cal

costs conducted at the request of CHA and in cooperation with the Health and Welfare Agency. The study, which estimated 1967-68 Medi-Cal costs on the basis of more recent data than available at the time of the original state estimates showed that:

- The net estimated Medi-Cal expenditures for the fiscal year 1967-68 are \$62 million less than the state's estimate of \$811 million.
- The Federal Medicare hospital reimbursement formula the state has been directed to adopt would cost Medi-Cal an additional \$7.5 million.
- The projected cost for physicians' services is \$24.5 million less than original state projections.
- The new estimates for county hospitals showed an increase of \$17.7 million over previous figures, while other hospitals showed a decrease of \$10.9 million.

Mr. Jackson expressed the hope that the CHA actuarial study would pave the way for early restoration of all benefits.

After speaking briefly about CHA concerns with problems relating to health manpower and comprehensive health planning, Mr. Jackson discussed the mutual problems relating to malpractice judgments and insurance. He invited CMA to join CHA in sponsoring an invitational conference which would attempt to develop solutions to current, common professional liability problems. Participants would be drawn from the medical profession, hospitals, insurance companies, the legal profession and others. Mr. Jackson suggested that the conference could be followed by a series of institutes throughout the state, which would bring the constructive thinking which evolved from the conference to individual physicians and hospitals. He emphasized that in all CMA and CHA concerns, a basic problem is communication with the "grass roots."

Concluding his remarks, Mr. Jackson expressed his appreciation to CMA for its cooperation during his two years in office.

ACTION: *Voted to join with CHA in sponsoring a conference on professional liability problems, allocating funds as necessary.*

13. *Health and Welfare Agency*

Mr. Spencer Williams of the State Health and Welfare Agency expressed his appreciation for the actuarial study conducted at the request of the California Hospital Association and reiterated the intent of the Administration to restore services as

soon as it can be seen that funds will be available.

Regarding abuses of the program, Mr. Williams stated that in his testimony before the Assembly Public Health Committee, he repeatedly pointed out that physician abusers of the Medi-Cal program represent only a fraction of the doctors rendering services under the program. He said that the Health and Welfare Agency welcomes CMA recommendations concerning withholding participation in the program from any specific physicians who have abused it.

In conclusion, Mr. Williams said that the administration hopes to have a better Medi-Cal Bill introduced in the 1968 session of the Legislature and encouraged CMA to lend its assistance in devising such legislation.

14. *Reports of Medical Schools*

Dean Warren Bostick of UC-California College of Medicine reported that all necessary legal arrangements had been completed so that his school could relocate on the Irvine campus in Orange County.

Doctor Robert Stowell, assistant dean of UC School of Medicine at Davis, stated that his school was continuing to enlarge its faculty, with 25 current faculty members, 11 expected by the first of the year, and six more scheduled to report a few months later. He also reported that over 200 applications have been received for enrollment in the first freshman class, which will begin studies in the fall of 1968. Applicant students are of very high caliber, Doctor Stowell stated, and 90 per cent are from California.

15. *State Department of Mental Hygiene*

Doctor Vernon Bugh, representing the State Department of Mental Hygiene, remarked on the two-fold long range plan of the department: to facilitate development of local programs and to increase the quality of care in existing state facilities. Eventually, he said, it was hoped that not only could both be improved but they also could be integrated. Doctor Bugh reflected upon the decreasing population of state mental institutions, but said that facilities for the mentally retarded have been slower in developing. An encouraging development, he said, is the creation of 500 new beds at the Camarillo facility in Ventura County.

16. *State Department of Public Health*

Doctor Lester Breslow, director of the State

Department of Public Health, commented briefly on developments relating to California implementation of Public Law 89-749 (Comprehensive Health Planning). He noted that the State's Comprehensive Health Planning Council has met twice, once for orientation purposes and once to approve the preliminary state plan. Two major issues in this area need to be resolved, according to Doctor Breslow. The first concerns the relationships between three levels of organization in California: statewide, regional and county. The second concerns the form of organization to be established at the regional and county levels where variation is expected. Doctor Breslow said that the most encouraging development in comprehensive health planning so far is the initiative being displayed by county medical societies. He pointed to San Diego, San Francisco, Sacramento, Los Angeles and Santa Clara as counties which have been especially active in providing leadership.

17. *Social Security Administration*

Mr. Keith Olson, assistant regional representative of the Bureau of Health Insurance, Social Security Administration, reported that the major concern of his Bureau at the moment was a currently pending bill which would change the open enrollment period for Medicare. The next open enrollment period is scheduled to begin 1 October and end 31 December. The bill would establish a new enrollment period to begin 1 January and end 31 March. Medicare enrollment would be open each year rather than every other year. Thus, he said, the Secretary would be able to establish a new premium rate each year based on the experience of the previous year.

Mr. Olson also reported that SSA had recently sent to carriers new guidelines for custodial care exclusion, which would be distributed widely. The new guidelines, he said, encourage looking to the level of service which a patient is receiving in an extended care facility as the major criterion. With these new guides, SSA hopes to reduce confusion in this area.

18. *California Nurses' Association*

Mrs. Helen Hancock, president of the CNA, said that her organization is looking forward to cooperating with CMA in presenting a special program highlighting health manpower at the coming CMA Annual Session.

19. California Medical Assistants Association

Miss Helen Goldman, president of CMAA, gave a brief preview of the 11th Annual Convention of the American Association of Medical Assistants, to be held October 11-15 at the International Hotel in Los Angeles.

20. Medi-Cal Developments

After extensive discussion, during which President Morrison presented background of recent developments concerning the Medi-Cal program and President-Elect Todd presented a proposed statement for dissemination to the membership, the Council made the following decisions:

ACTION: *Voted to approve a statement reaffirming belief in the concept of "mainstream" medical care and pledging efforts to restore usual and customary fees, as well as other necessary services, to the Medi-Cal program, to be included in a letter to the CMA membership (text of approved statement is below).*

"The Council of the California Medical Association reaffirms its belief in the mainstream concept of medical care, that health services for Medi-Cal recipients should be directly related to the needs of the patient and should be identical to that available and received by the public at large.

"The Council is concerned with curtailment of necessary health care services for needy citizens covered by the Medi-Cal program and urges appropriate restoration at the earliest opportunity.

"The CMA Council has been informed that California Blue Shield, as fiscal intermediary, has been directed by the State of California to reduce the level of payment for physician services under the Medi-Cal program to a level below that of usual fees. CMA recognizes that California Blue Shield has no alternative but to execute this directive.

"The Council affirms its conviction that such reductions will cause discrimination against some Medi-Cal patients. We have been informed that this is a temporary fiscal expediency. CMA will continue to work for a restoration of the usual and customary fee concept, as well as other necessary services."

ACTION: *Voted to recommend to the Health and Welfare Agency that primary consideration be given to modifying the new Medi-Cal regulations that affect hospital stays, surgery, dental care, psychiatric care, and the drug formulary, so that all five of these services might be restored to the program.*

ACTION: *Voted to establish an ad hoc Committee on Medi-Cal, designed to study and make recommen-*

dations concerning the future of the Medi-Cal program (to consist of the Committee for Emergency Action and Doctors Boyle, Bullock, Fenlon, Shapiro and R. Wilbur).

21. CMERF Studies

Following up on Council action of 26 August 1967, requesting the Board of Directors of the California Medical Education and Research Foundation to consider and act on the question of pre-evaluating studies, Doctor Morrison, chairman of the CMERF Board, reported that the following statement had been adopted:

"The Board of Directors of CMERF has considered the action of the Council and will be mindful, in advance, of all potential problems inherent in the conduct of various studies, including the publication of the results thereof."

22. Postgraduate Institutes

The Council's attention was directed to a request from the Scientific Board for approval to raise the fees for CMA Regional Postgraduate Institutes from \$15 to \$20 per institute—to cover more nearly the increased costs of instruction.

ACTION: *Voted to approve increasing fees for CMA Postgraduate Institutes from \$15 to \$20 per institute.*

Councilor Yant read a letter from Doctor James W. Martin, president of Sacramento County Medical Society, requesting that CMA change the location and date of the annual CMA Sacramento Valley Postgraduate Institute so that it might coincide with the Society's activities commemorating their centennial year.

ACTION: *Voted to approve cooperating with Sacramento County Medical Society in presenting a scientific seminar on May 4-5, 1968, in Sacramento.*

23. Professional Liability Problems

On behalf of the Medical Review and Advisory Committee, Chairman Yant presented a summary of its meeting with representatives of the American Mutual Liability Insurance Company and northern county medical societies. The meeting focused on the rapid increases in rates for malpractice insurance, resulting from the large losses recently being experienced by insuring agencies. To help alleviate this problem, three areas which need greater attention were pinpointed:

a. The positive image—Medicine must project this and avoid being negative.

b. Doctor-patient relationship—This is still the most important factor in preventing suits.

c. Legislation—Ultimate relief may be found here. Not only physicians but attorneys, architects, engineers, etc., are evidencing concern in this area.

Legal Counsel Hassard discussed Senate Resolution No. 356, introduced into the last session of the Legislature, passed by the Senate and referred to the Committee on Rules for study. The resolution deals with medical malpractice insurance, medical standards and grounds for a medical malpractice suit. With the first hearing scheduled for 17 October, Mr. Hassard urged the Council to give prompt consideration to the "legislative platform" outlined in the written report of the Medical Review and Advisory Committee. As a basis for supporting legislative action in this area, the following points were offered:

a. Elimination of the doctrine of *res ipsa loquitur* (the case speaks for itself). This is commonly known as the "rule of sympathy" and has been to some degree responsible for juries awarding large settlements in some cases.

b. A realistic statute of limitations should be established. It is now one year after the date or cause of action arises. However, quite some time ordinarily elapses before settlement is finally made, predicated on the "going rate."

c. "Informed consent" should be more clearly defined. One of the biggest problems in this area is failure on the part of a physician to explain to his patient the risk involved in a certain procedure or treatment.

d. Immunity from discovery for proceedings, reports and decisions of county review committees.

e. Immunity for physicians and committee members reporting a fellow physician to the Board of Medical Examiners.

f. Fast payment of claims without admission of liability on the part of the carrier. It is recommended that at the time of the hearing on this subject re automobile claims, which is set for 6 October, efforts be made to have professional liability included.

g. Ceiling on damages. It was suggested that perhaps a "sliding scale of injuries" or judgment by an independent body might be possible solutions.

ACTION: *Voted to approve the above "seven-point" program as a basis for CMA efforts to improve medical malpractice legislation.*

24. *Commission on Communications*

In the absence of Chairman Goel, Councilor Roberta Fenlon called to the attention of the Council the written informational report of the Commission on Communications included in the Council notebook. The report outlined results of the 6 September 1967 meeting of the Commission. The Commission gave a preliminary report on House of Delegates actions referred to it and outlined several areas to which it was giving increased attention: evaluation of current methods to communicate with physicians, expansion of field service function, and counteraction of public misunderstanding regarding physician charges.

Councilor Homer Pheasant suggested that communication with medical staffs could be improved by setting up a specific bulletin board location for news from CMA.

25. *Medical Executives Conference*

Chairman Eldon E. Geisert briefly commented on the Friday, 29 September 1967, meeting of the Medical Executives Conference, pointing out that the morning session had been devoted to a productive exchange of ideas with representatives of California Blue Shield, including Mr. Thomas Paton, Blue Shield president.

26. *Woman's Auxiliary to the CMA*

Mrs. Dorothy Flood, president of the Woman's Auxiliary, commented briefly on the recent Fall Conference, which, she said, is really an "annual workshop." More persons registered for the meeting than in any past year. Mrs. Flood thanked all those who contributed to the success of the meeting, including Doctors Morrison and Todd and staff of CMA, the Public Health League, AMPAC and CALPAC.

27. *Report of Legal Counsel*

Legal Counsel Hassard reported that not all of the Medi-Cal regulations that were filed to become effective on 1 September are affected by the court's injunction, and that a document would be forthcoming soon from the Office of Health Care Services listing those regulations that are affected as well as those which are not. Mr. Hassard also stated that the Supreme Court will be hearing oral arguments on the case on Wednesday, 1 November 1967, and said that CMA Legal Counsel may submit a brief in advance of that time.

28. *Staff Report*

Executive Director Robert L. Thomas distributed to the Council booklets outlining the organizational structure of the CMA staff. The booklet also contains several sample position descriptions; similar job profiles are being prepared for all staff members. In addition, Mr. Thomas stated that CMA has produced an "Employee Handbook" outlining personnel policies of the Association and said that he would be happy to send a copy to any Councilor requesting it.

Mr. Thomas regretfully announced the resignation of Mr. William Whelan, associate executive director, stating that Mr. Whelan would be retained on a consulting basis for about a year. On behalf of the staff, Mr. Thomas extended best wishes to Mr. Whelan in his future endeavors.

On behalf of the officers and the Council, President Morrison expressed deepest appreciation to Mr. Whelan for his outstanding contributions to the work of the Association.

Mr. Whelan said that he was extremely grateful for having had the opportunity to work with the dedicated CMA staff and physician leadership during the past eight years.

29. *Membership Report*

Six applicants were voted election to Associate Membership. These were: John A. Blosser, Robert L. Christensen, Hubert F. Zappas, Alameda-Contra Costa County; Harry Morris Bauer, Allan Maxwell Warner, Los Angeles County; Thomas Phillip Johnson, San Diego County.

Four members were voted election to Retired Membership. These were: Harold P. Totten, Los Angeles County; Robert Rosen, San Diego County; J. Paul Sweeney, San Mateo County; Walter Freeman, Santa Clara County.

Reduction of dues was voted for nine members for reasons of prolonged illness or postgraduate education.

30. *Roll Call*

Present were President Morrison, President-Elect Todd, Speaker Quinn, Vice-Speaker Boyle, Secretary Weyrauch, and Councilors Moore, Eastman, Woolington, Pheasant, Bullock, O'Connor, Shapiro, Rogers, Crum, Watson, Maguire, Burnett, Miller, Richard Wilbur, Watts, Fenlon, Rose, Yant, Grunigen and Immediate Past President MacLaggan.

Present by invitation were CMA staff members Borgfeldt, Bowman, E. Collins, J. Collins, Curley, Eberlein, Goldman, Griffith, Hetland, Klutch, Lemos, Miller, Price, Redfern, Schallenberger, Thomas and Whelan; Messrs. Hassard and Huber, Legal Counsel; Component Society Executives Scheuber of Alameda-Contra Costa, Rideout of Butte-Glenn, Garrick of Forty First, Lingerfelt of Fresno, Geisert of Kern, Brock of Imperial, Dalbec of Los Angeles, Sower of Marin, Colvin of Monterey, Blough of Orange, Dochterman of Sacramento, Donmyer of San Bernardino, Jackson of San Diego, Neick of San Francisco, Wood of San Mateo, Marvin of Santa Barbara, Donovan of Santa Clara and Bruce of Tulare; Messrs. Paton, Babb, Clark, Koch and Potloff of California Blue Shield; Messrs. Read, Brown and McWilliams of the Public Health League; Dean Bostick of UC-California College of Medicine; Assistant Dean Stowell of UC School of Medicine at Davis; Mr. Williams of the Health and Welfare Agency; Doctor Rosen of the Office of Health Care Services; Doctor Breslow of the State Department of Public Health; Doctor Bugh of the State Department of Mental Hygiene; Doctor Skelly of the State Department of Social Welfare; Doctor Coombs and Del Junco of the State Board of Medical Examiners; Mr. Olson of the Bureau of Health Insurance, Social Security Administration; Mr. Gould of the AMA Staff; Mrs. Hancock of the California Nurses' Association; Miss Goldman of the California Medical Assistants Association; Mrs. Flood of the Woman's Auxiliary to CMA; Doctors Axelrod, Blanchard, Bueger, Davis, Elliott, Hill, Hull, Judd, Kiddie, Mailman, McDonald, Pitchford, Schroeder, Spaulding, Tabellario, Tudbury, Wanless and others.

31. *Next Meeting of the Council*

Chairman Miller announced that the next regular meeting of the Council would be held on Saturday, 4 November, at the Hilton Inn, San Francisco, with a special executive session scheduled for the previous evening.

32. *Adjournment*

The meeting was adjourned in memory of Wayne Pollock, M.D., on Saturday, 30 September 1967 at 4:45 p.m.

ALBERT G. MILLER, M.D., *Chairman*

HELEN B. WEYRAUCH, M.D., *Secretary*

Plan NOW to Attend

CALIFORNIA MEDICAL ASSOCIATION

1968 ANNUAL SCIENTIFIC ASSEMBLY

FAIRMONT AND MARK HOPKINS HOTELS • SAN FRANCISCO

March 23–27

Four General Sessions on

- THE MANY PROBLEMS OF BLOOD
- PROBLEMS IN DRUG ABUSE
- TRAUMA: PREVENTION, CAUSES, TREATMENT
- NEW DRUG THERAPY AND REACTIONS

RENOWNED SPEAKERS ARE:

JAMES H. CAVANAUGH, Ph.D.

Director
Office of Comprehensive Health Planning
Office of the Surgeon General
United States Public Health Service

JAMES L. GODDARD, M.D.

Commissioner
Food and Drug Administration

CHARLES A. CHIDSEY, III, M.D.

Associate Professor of Medicine
Head, Section on Clinical Pharmacology
University of Colorado School of Medicine

CECIL HOUGIE, M.D.

Associate Professor of Pathology
University of Washington School of Medicine

DANIEL DEYKIN, M.D.

Assistant Professor of Medicine
Harvard Medical School

TOD H. MIKURIYA, M.D.

Consultant
Center for Narcotics and Drug Abuse Studies
National Institute of Mental Health

JOHN A. OATES, M.D.

Associate Professor Medicine and Pharmacology
Vanderbilt University School of Medicine

EIGHTEEN SCIENTIFIC SECTION PROGRAMS ON A VARIETY OF TOPICS

Special Conferences Include:

Conference on Physicians and Schools
A Joint Conference with California Nurses Association on Problems in Manpower
L. Henry Garland Memorial Lecture
Alice Stone Woolley Memorial Lecture

PLUS OUTSTANDING SCIENTIFIC AND TECHNICAL EXHIBITS

application for **HOTEL ACCOMMODATIONS**

NINETY-SEVENTH *Annual Session*

CALIFORNIA MEDICAL ASSOCIATION • MARCH 23-27, 1968

FAIRMONT AND MARK HOPKINS HOTELS, SAN FRANCISCO

House of Delegates Opening Session, Mark Hopkins, Saturday evening, March 23;

Scientific Sessions, Fairmont Hotel, begin Sunday morning, March 24.

1. Fill in the form below **completely** for room accommodations at the CMA's 1968 Annual Session. There is only a limited number of rooms available. Your choice of accommodations will be better if your request is for rooms to be occupied by two or more persons.
2. Your reservation request should include the definite date and hour of your arrival and departure.
3. All reservations must be made through the CMA Housing Bureau, Fox Plaza—Suite 260, San Francisco, California 94102 by *March 1, 1968*.

HOTEL ROOM RATES*

| | Single | Double and Twin | Suites |
|-----------------------------------------------------|---------|--------------------|----------|
| FAIRMONT — Atop Nob Hill..... | \$18-34 | \$23-39 | \$45-114 |
| MARK HOPKINS — Atop Nob Hill..... | 18-29 | 23-34 | 48- 90 |
| HUNTINGTON 1075 California | None | 21-35 | 55- 95 |
| ST. FRANCIS Powell and Geary | 16-31 | 20-36 | 45-110 |
| SIR FRANCIS DRAKE Powell and Sutter | 15-22 | 19-26 | 70 |
| HANDLERY INN 260 O'Farrell | 20-26 | 24-30 | None |
| CHANCELLOR HOTEL 433 Powell | None | 13-15 | None |
| PLAZA HOTEL Post and Stockton | None | 14-17 | None |

*Rates subject to change

Send to: CALIFORNIA MEDICAL ASSOCIATION—*Housing Bureau*
Fox Plaza, Suite 260, San Francisco, California 94102

Please reserve the following accommodations for the CMA's 1968 Annual Session in San Francisco, March 23-27. House of Delegates Opening Session, Saturday, March 23, at the Mark Hopkins; Scientific Programs begin Sunday morning, March 24, at the Fairmont.

Single Bedroom \$.....Twin-Bedded \$.....Double Bed \$.....

Small Suite \$.....Large Suite \$.....Other \$.....

First Choice Hotel.....Second.....Third.....

Arrival (date).....Hour.....a.m.
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p.m.

THE NAME OF EACH HOTEL GUEST MUST BE LISTED. Include the names and addresses of each person in a double or twin-bedded room, and names and addresses of all other persons for whom you are requesting reservations.

—PLEASE PRINT OR TYPE—

Your Name:.....Officer?.....Delegate?.....Alternate?.....Speaker?.....

Address:.....County.....

City and State.....Zip.....

Suggested Solutions Planning and Goals

RICHARD W. OPFELL, M.D.

*Chairman, Postgraduate Committee
Orange County Medical Association*

THE TIME HAS COME to put into action the recommendations of the Planning and Goals Conference in Continuing Medical Education (see CALIFORNIA MEDICINE, August and September 1967). The entire program as presented may seem difficult to implement, especially on a state-wide basis.

The following suggestions are offered as a way to get started now:

I. "The Role of Hospitals" Every community hospital is required to audit the work done in the hospital. The audit should become an educational exercise and not police work.¹ The audit should be systematic, based on individual diagnoses, and consist of comparing the professional care rendered with criteria developed previously to insure uniform evaluation of the quality of care and of appropriate utilization of the hospital and hospital services.

Criteria have been developed for more than 50 disease entities to measure both quality of care and effectiveness of the use of the hospital.² The use of the audit as an educational device should be supplemented by systematic educational programs selected in the light of demonstrable needs. The program should be innovative and include lectures, clinical pathological conferences, symposia, distribution of literature, Audio-Digest, television, and staff newsletters. Help could be obtained for the educational program from medical schools, local medical societies, and California Medical Association.

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II. "Evaluation" In this system evaluation of the results of the educational effort is automatic by comparing data continually produced by the audit. Hospitals can be compared with one another if similar criteria were used.

III. "Motivation" Motivation is also built into this system. Every physician likes to feel that he practices high-quality medicine. Unfortunately, many current audits let pass all but the most outrageous and flagrant examples of poor practice, thereby implying that mediocre practice is acceptable. The involvement of the medical staff in the educational audit would rectify this problem by its effort to insure uniform high-quality medical care. Service on the audit committee is a recognized duty of all staff members and could be made a requirement for continuation of hospital privileges.

IV. "Certification or Accreditation" The CMA survey team would have access to the educational audit and could readily determine the effectiveness of each hospital's program of continuing medical education. If identical criteria were used, the survey teams would be better able to determine the quality of medical care and appropriate hospital utilization.

These suggestions are offered as a coordinated program to implement the recommendation of the Planning and Goals Conference. By making better use of the time physicians already devote to the necessary committee work of the community hospital, any hospital or county medical association can start now.

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2. Payne, Beverly C.: Continued evolution of a system of medical care appraisal, JAMA, 201:536-540, 14 Aug. 1967.

In Memoriam

ABDO, FRANCIS JOSEPH, Los Angeles. Died 2 November 1967 in Los Angeles of myocardial infarction, aged 57. Graduate of Rush Medical College, Chicago, Illinois, 1937. Licensed in California in 1939. Doctor Abdo was a member of the Los Angeles County Medical Association.



BERMAN, PHOEBUS, Pasadena. Died 24 October 1967 in Pasadena of myocardial infarction, aged 77. Graduate of College of Physicians and Surgeons, Medical Department, University of Southern California, 1919. Licensed in California in 1919. Doctor Berman was a member of the Los Angeles County Medical Association.



BRIGHAM, FRANK OTIS, Los Angeles. Died 2 November 1967 in Los Angeles of cerebral infarction, aged 82. Graduate of Bennett College of Eclectic Medicine and Surgery, Chicago, Illinois, 1908. Licensed in California in 1922. Doctor Brigham was a retired member of the Los Angeles County Medical Association and the California Medical Association, and an associate member of the American Medical Association.



CECIL, ARTHUR BOND, Los Angeles. Died 11 October 1967 in Los Angeles of myocardial failure, aged 82. Graduate of Johns Hopkins University School of Medicine, Baltimore, Maryland, 1909. Licensed in California in 1913. Doctor Cecil was a member of the Los Angeles County Medical Association.



CHOCK, CHONG AUCK, Los Angeles. Died 13 October 1967 in Los Angeles of coronary thrombosis, aged 60. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1936. Licensed in California in 1936. Doctor Chock was a member of the Los Angeles County Medical Association.



DELPRAT, JESSIE LUNT PREBLE, San Francisco. Died 24 October 1967 of cerebral vascular accident, aged 77. Graduate of the University of California School of Medicine, Berkeley-San Francisco, 1923. Licensed in California in 1923. Doctor Delprat was a member of the San Francisco Medical Society.



GIANETTI, JOHN, Santa Ana. Died 8 November 1967 in an airplane crash near Salinas, aged 41. Graduate of Wayne State University College of Medicine, Detroit, Michigan, 1959. Licensed in California in 1960. Doctor Gianetti was a member of the Orange County Medical Society.

GEISLER, WILLIAM H., San Jose. Died 4 November 1967 in San Jose, aged 67. Graduate of Northwestern University Medical School, Chicago, 1927. Licensed in California in 1929. Doctor Geisler was a retired member of the Santa Clara County Medical Society and the California Medical Association, and an associate member of the American Medical Association.



HARMS, HERBERT ERIC, San Leandro. Died 12 October 1967 in Livermore of acute myocardial infarction, aged 61. Graduate of the University of Colorado School of Medicine, Denver, 1932. Licensed in California in 1939. Doctor Harms was a member of the Alameda-Contra Costa Medical Association.



KELLOGG, RAYMOND P., Lake San Marcus. Died 27 October 1967 in San Gabriel of coronary thrombosis, aged 66. Graduate of College of Osteopathic Physicians and Surgeons, Los Angeles, 1927. Licensed in California in 1928. M.D. degree from California College of Medicine, 1962. Doctor Kellogg was a retired member of the Los Angeles County Medical Association and the California Medical Association, and an associate member of the American Medical Association.



KLICK, JOHN JOSEPH, Santa Cruz. Died 8 October 1967 in Santa Cruz, aged 86. Graduate of Rush Medical College, Chicago, 1905. Licensed in California in 1912. Doctor Klick was a member of the Sacramento County Medical Society, a life member of the California Medical Association, and a member of the American Medical Association.



MANDELL, JOSEPH, Los Angeles. Died 17 August 1967 in Los Angeles of Hodgkin's Disease, aged 58. Graduate of the University of California School of Medicine, Berkeley-San Francisco, 1935. Licensed in California in 1935. Doctor Mandell was a member of the Los Angeles County Medical Association.



MICKLIN, MYER JEROME, Northridge. Died 17 October 1967 in Northridge of cerebral infarction, aged 53. Graduate of Temple University School of Medicine, Philadelphia, Pennsylvania, 1947. Licensed in California in 1948. Doctor Micklin was a member of the Los Angeles County Medical Association.



ROST, PAUL C., Los Angeles. Died 19 October 1967 in Germany of cerebral vascular accident, aged 75. Graduate of Georg August-Universität Medizinische Fakultät, Göttingen, Prussia, Germany, 1920. Licensed in Cali-

fornia in 1942. Doctor Rost was a member of the Los Angeles County Medical Association.



SHERTER, CHARLES, Lakewood. Died 8 October 1967 in San Gabriel of myocardial infarction, coronary arteriosclerosis, aged 47. Graduate of the University of California School of Medicine, Berkeley-San Francisco, 1945. Licensed in California in 1945. Doctor Sherter was a member of the Los Angeles County Medical Association.



TIEDEMAN, IAN DAVIS, Whittier. Died 10 October 1967 in Whittier of bronchopneumonia, aged 77. Graduate of the University of Illinois College of Medicine, Chicago, 1916. Licensed in California in 1927. Doctor Tiedeman was a retired member of the Los Angeles County Medical Association and the California Medical Association,

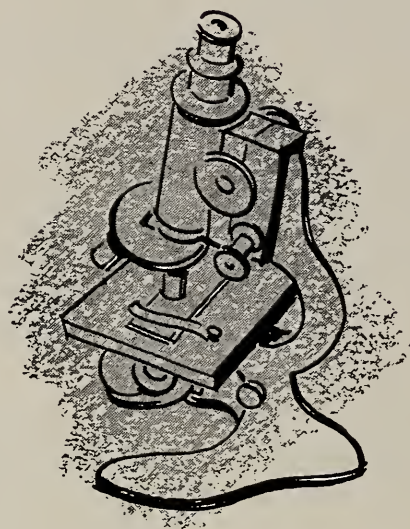
and an associate member of the American Medical Association.



WELPTON, MARTHA ANNA, San Diego. Died 13 August 1967 in San Diego of arteriosclerotic cardiovascular disease, aged 83. Graduate of Rush Medical College, Chicago, Illinois, 1910. Licensed in California in 1917. Doctor Welpton was a retired member of the San Diego County Medical Society and the California Medical Association, and an associate member of the American Medical Association.



WILSON, GEORGE W., Los Angeles. Died 19 October 1967 in Los Angeles of bronchiectasis, aged 76. Graduate of Wayne University College of Medicine, Detroit, Michigan, 1914. Licensed in California in 1953. Doctor Wilson was a member of the Los Angeles County Medical Association.



PUBLIC HEALTH REPORT

Lester Breslow, M.D., M.P.H.

Director, State Department of Public Health

PKU Testing

CALIFORNIA IS ONE OF 38 states that currently have legislation on testing for phenylketonuria (PKU). Implementation of the California law is somewhat unique in that the usual channels of medical care and laboratory services do the testing of newborns that is required, rather than a single or several central laboratories under state sponsorship as is the practice in many other states. Here the state and local health departments record the results of testing and the number and kind of services provided.

In 1966, in excess of 90 per cent of California's 330,000 newborns had blood phenylalanine determinations performed. There were 1,162 infants with positive results (that is, 4 mg or more per 100 ml) on their first test, a rate of about three positives per 1,000 tests. Approximately 90 per cent of these were retested as the regulations require and 162 were positive on the second test. Of these 162 infants with two positive tests, 16 were eventually found to be phenylketonuric. These figures indicate that there is an acceptably low number of false positive tests—that is, positive test results in the absence of the disorder. Follow-up to arrive at a definitive diagnosis, when the initial positive result has alerted the physician to this possibility, is often difficult but has been carried out in California at a high level of completeness.

Through testing in the first half of 1967 an additional 12 cases in approximately 150,000 births have been discovered. In the first half of 1966, 2,805 infants were reported as discharged who, for various reasons, had not had the test. This represented approximately 2 per cent of the births. Reports for the first half of 1967 indicate

that only 1,155 infants (less than 1 per cent of the births) were discharged without testing.

The physicians of the state have assumed a central role in the success of this testing program. At the time the testing program was initiated, some anxiety was expressed that infants would be prematurely placed on the restrictive therapeutic diet on the basis of a single screening test result. This has not occurred. The regulations require that a repeat test be performed in all cases in which the first test is positive. Only after a second positive test is the infant eligible for a Crippled Children Services-supported diagnostic evaluation; and only after the best medical judgment has been rendered is the diet prescribed. The physicians of the state have supplied the medical judgment necessary to the proper implementation of the law by separating out the other causes of elevated blood phenylalanine from PKU.

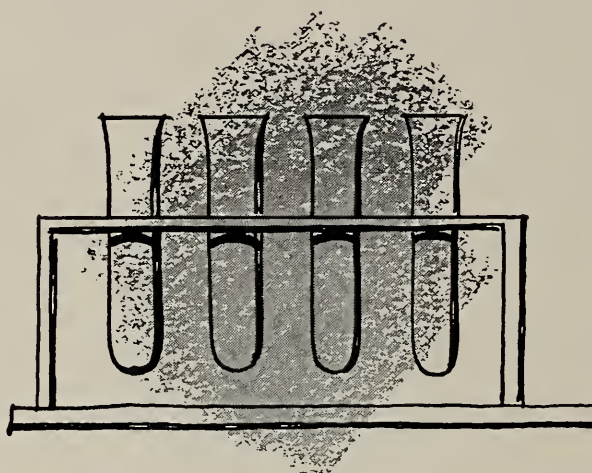
Some anxiety was also expressed that the setting of an arbitrary reporting level (4 mg per 100 ml) might lead to its use as a rigid diagnostic criterion. The experience shows that the true meaning of the positive screening level has been widely recognized. In many instances repeat testing has been performed where the initial test showed a borderline result, thus removing any question of the possibility of PKU. The influence of the time of the test, the feeding history and the type of test are all factors that must be used in the interpretation of these borderline results.

Two infants in whom PKU was ultimately diagnosed had negative initial newborn tests. The first of these, born in 1966, was a term infant tested at three days of age, following breast and bottle feeding for 48 hours. A Guthrie test was read at less than 2 mg per 100 ml. The second infant, born in 1967, was also a term infant whose Guthrie test was reported also as 2 mg per 100 ml on the fourth day of life.

The State Department of Public Health has accumulated an appreciable amount of information about the disorder and the tests used to detect it. This information is available to the medical profession.

A registry with information on the more than 350 patients with PKU currently residing in California has been developed. The Department has also cooperated in a collaborative study of phenylalanine loading tests on infants with high levels, and their parents and siblings. Staff members are participating in a national study on most effective use of the diet.

The effect of this legislation has been an increase in the completeness with which newborns receive PKU screening tests. In a significant number of California-born children, mental retardation has been thus prevented through early diagnosis and treatment. Although controversial at times, the medical knowledge about PKU has been increased decidedly in recent years as the result of newborn screening and treatment of patients with the disorder, and as improved techniques for diagnosis are developed and rapidly introduced into practice.



WOMAN'S AUXILIARY

to the California Medical Association



International Health Activities

DOCTOR, If you truly believe in "Better Health for a Better World," you will let *I Have Aided* be your motto for 1967-1968.

A major project of the Woman's Auxiliary to the CMA is the continued support of its program, "International Health Activities." This program is dedicated to the fulfillment of international self-help to health, thus making it possible for participation of each member through support of the many diversified outlets covered by the broad scope of the project.

During the past year, participation in the International Health Activities by the WACMA brought about the collection of 68,000 pounds of surplus pharmaceuticals as well as 410 pounds of medical and surgical equipment sent to Direct Relief Foundation in Santa Barbara. In addition, 39,039 pounds of surplus pharmaceuticals were shipped to various individual medical outlets as requested by the donors; World Medical Association was the recipient of 224 journals, 37 textbooks, and 400 pounds of medical equipment.

This collection represents an invaluable amount of aid for those in need, as well as a well-organized, concerted effort on the part of your auxiliary. "Project Hope," "AMDOC," "Doctor to Doctor" and International Hospitality programs have been actively supported.

Doctor, keep those medical supplies going overseas. At present it takes approximately 4,000 pounds of medical supplies (surplus drugs, medical and surgical instruments, bandages, "johnny coats" and the like) *each day* to fill existing requests made to Direct Relief Foundation in Santa Barbara alone.

At this date, we are formulating a program in conjunction with the California Medical Assis-

stants' Association to make this endeavor a joint project. Thus, you will be besieged at home by your wife and at the office by your assistant to participate by donating surplus drugs, medical and surgical instruments, and medical supplies—as well as your old shirts.

All collections are sent to a responsible collection agency, registered with the U.S. Food and Drug Administration, licensed by the appropriate health agencies of the State of California, which maintains its operations under the supervision of a registered pharmacist and has the necessary export licenses permitting shipment of drugs overseas.

No contributions are sent abroad except to legitimate medical missions or hospitals (upon proper request by a physician), and only then after each shipment is properly sponsored. Nothing is sent overseas without rigid investigation as to the validity of the request.

Present programs include:

Medical Supplies

1. Surplus pharmaceuticals, medicines, vitamins (original, sealed packages).
2. Baby foods (unopened cans or containers).
3. Medical supplies, instruments, x-ray equipment.
4. Artificial limbs, braces, crutches, sheets, blankets, towels.
5. Clean, old sheets (torn into 2- or 3-inch strips for bandages), packaged in plastic bags.
6. Clean, used shirts (for "johnny coats").
7. Office furniture and equipment.
8. Dental supplies, instruments, dental x-ray equipment.

Guide lines as set up by the Woman's Auxiliary to the American Medical Association prepared by the Judiciary Council of the AMA and ap-

proved by the U.S. Food and Drug Administration must be followed. Sample drugs should be collected from the physician's office in their original, unopened packages. These samples should be put in a carton, sealed, and sent to a responsible collection agency. Drugs collected by the auxiliary shall not be sent directly overseas.

Items of the kind listed above should be sent to either:

DIRECT RELIEF FOUNDATION

27 E. Canon Perdido Street
Santa Barbara, Ca. 93101

or

PROJECT CONCERN, INC.

P. O. Box 2468
San Diego, Ca. 92212

Medical Services

Doctor to Doctor. This program has two functions—to provide *current* medical literature to overseas physicians who cannot obtain it otherwise, and to open up avenues of communication between all physicians and their overseas colleagues, establishing thereby a basic medium for better understanding.

Write to:

Ada Chree Reid, M.D., Chairman
American Medical Association
"DOCTOR-TO-DOCTOR PROGRAM"
c/o The World Medical Association, Inc.
10 Columbus Circle, New York, N.Y. 10019

AMDOC, an exchange services program, arranges for physicians, nurses, and paramedical members to be sent overseas to areas of need. (Short-term period of service; transportation and housing furnished in exchange for services.)

Write to:

AMDOC
27 E. Canon Perdido Street
Santa Barbara, Ca. 93101

Medical Teaching. This program is to supply help in administering medical teaching programs for newly emerging nations. Under it, service has been supplied in Indonesia, South Vietnam, Peru, Ecuador, Guinea, Nicaragua, and Colombia.

Write to:

PROJECT HOPE
Wm. B. Walsh, President
2233 Wisconsin Avenue, N.W.
Washington, D.C. 20007

MED-AID—instructions via short-wave radio. MED-AID operates a daily short-wave medical

emergency service which connects Durham, N.C., with isolated medical outposts throughout the world. Calls have come from Bolivia, Peru, Ecuador, Costa Rica, Nicaragua, Honduras, Guatemala, San Salvador, Mexico, Liberia and the Congo. Instantaneous consultation on the latest diagnosis, treatment, and prevention of disease is available through the skills of medical specialists in institutions at Duke University. MED-AID and AMDOC are cooperating.

MARCO is securing equipment for setting up ham radio stations for MED-AID. If ham radio equipment or useful parts for building ham radios are available (gratis), write to:

Dr. Wm. Sprague
433 North 4th St.,
Montebello, Ca. 90640

Volunteer Physicians for Vietnam. Physicians who volunteer services for specific period—transportation and housing plus \$10 per day expenses.

Write to:

**AMA VOLUNTEER PHYSICIANS
FOR VIETNAM**

535 North Dearborn Street
Chicago, Ill. 60610

Vietnamese Student-Aid Project. Training students to return and work and train others for the Saigon Medical School. Needs financial aid.

Send check to:

Woman's Auxiliary to the AMA
535 North Dearborn Street
Chicago, Ill. 60610

earmarked for "Vietnamese Student-Aid Project.

International Hospitality. Through International Medical Family Days, arrangements are made for entertainment of visiting foreign physicians and wives; for dissemination of information to physicians' wives in foreign countries; for invitations to foreign medical students' wives to WA-SAMA and to all Auxiliary meetings. Other functions are to promote foreign students' programs, visit international clubs and tell of the Auxiliaries' programs in International Health Activities and how they can help their own countries' health progress.

Doctor, please clip and save this article as a handy reference to assist you in actively participating in this tremendously necessary, worthwhile program sponsored by *your* Medical Auxiliary.

All donations are tax deductible with the exception of surplus pharmaceuticals.

MRS. CHARLES J. HART, *Chairman*
International Health Activities

The Physician's BOOKSHELF



CALIFORNIA MEDICINE does not review all books sent to it by the publishers. A list of new books received is carried on page 22 of the Advertising Section.

GREAT IDEAS IN THE HISTORY OF SURGERY—Second Revised Edition—Leo M. Zimmerman, M.D., Professor and Chairman, Department of Surgery, Chicago Medical School; Attending Surgeon, Michael Reese Hospital; and Ilza Veith, M.A., Ph.D., Professor and Vice-Chairman, Department of the History of Health Sciences University of California, San Francisco Medical Center. Dover Publications, Inc., 180 Varick St., New York, N.Y. (10014), 1967. 587 pages, \$3.00 (Paperback).

True comprehension of medicine requires knowledge of the history of medicine. Not only will the student be enriched by this knowledge: His insight into day's medicine will be enhanced. The popular edition of *Great Ideas in the History of Surgery* is a welcome addition to the paperback library of medicine. The authors wisely included many quotations of some of the historically as well as clinically important documents. It becomes obvious how, centuries ago, medical men were nonetheless able to make and describe observations which cannot be improved upon to this day.

Perhaps more space should have been devoted to Vesalius because of his importance as a trailblazer in the science of medicine.

In the modern era, little or no mention is made of vascular surgery. Already at the time of the hardcover publication of this book in 1961, this field of surgery had gained considerable stature.

The text is well written and easy to read. The Dover Press is to be complimented for making it available at a price which is within the reach of every medical student. To the advanced student of medicine and surgery the book is recommended as well. Not only will it increase his basic understanding of surgery, it also may have a sobering effect to realize that successful plastic surgery was done in Italy in the sixteenth century, while technically beautiful rhinoplasties were performed in India some two hundred years ago!

LEO VAN DER REIS, M.D.

* * *

FOOT DISORDERS—Medical and Surgical Management—Nicholas J. Giannestras, M.D., Department of Orthopaedic Surgery, University of Cincinnati, College of Medicine, Cincinnati, Ohio. Lea & Febiger, 600 S. Washington Square, Philadelphia, Pa. (19106), 1967. 521 pages, \$22.00.

Dr. Giannestras has brought together an impressive array of contributors to this work covering so many of the common problems an orthopedist sees in his day to day practice. The normal anatomy and biomechanics of the foot is clearly presented as a framework to which variations can be referred. The chapters on surgery of the rheumatoid foot, hallux valgus and neurological disorders are excellent and relatively complete. The recommended treatment for talipes equinovarus with adhesive strapping to a progressively angled bar will leave adherents to Dr.

Kites' tenets in dismay but ought to be presented as an alternative.

Treatment of the valgus foot, including the congenital rigid flat foot or vertical talus, is well worth reading as a report of an enthusiast for the conservative, active treatment of these conditions. Many orthopedists will feel too much emphasis is given to shoe correction as being truly corrective measures, but the proper use of heel and sole wedges and navicular and the "comma shaped pad" is a valuable adjunct to the symptomatic treatment of selected conditions. The Whitman footplate is appropriately recommended.

Many vexing problems are presented and solutions are recommended which the student or younger orthopedist will find invaluable. The book will not rank with Bunnell's *The Hand*, but comes as close as any so far produced and should be included in the library of anyone without already fixed ideas on the many time consuming problems related to the foot.

JEROME C. BEATIE, M.D.

* * *

GASEOUS DIGESTIVE CONDITIONS — Including Belching, Bloating, "Wind" and Air Swallowing — What They Are, What Causes Them and How They Can Be Controlled — Joseph H. Pollock, M.D., F.I.C.S., Department of Surgery, Cedars of Lebanon Hospital, Cedars-Sinai Medical Center, Los Angeles, California. Charles C Thomas, Publisher, 301-327 East Lawrence Avenue, Springfield, Ill. (62703), 1967. 163 pages, \$7.00.

Although interestingly written, this small volume only continues to confuse an already confused subject. The author discusses some common symptoms seen in a multitude of disorders (from peptic ulcer to hemorrhoids) and then brings these disorders together under the heading of "Gaseous Digestive Conditions." In January 1967, the New York Academy of Sciences held a conference on the subject of gastrointestinal gas. The scientific approach presented by the discussants at that conference stands in marked contrast to what this book offers.

This book is written primarily for the layman. However, it contains many ideas based more on folklore than on scientific study. It is dubious if such concepts as food allergy as a cause of gas, coupled with instructions for setting up an elimination diet to treat this, should be widely disseminated to the laity. The last section of the book is designed for the physician but is little more than a brief description of the categories into which drugs used in the treatment of gastrointestinal disease fall plus a long list of these drugs. It would appear, therefore, that this book offers little of significant value to the physician.

PAUL H. GUTH, M.D.

TEXTBOOK OF GYNECOLOGY—Fourth Edition—John I. Brewer, B.S., M.D., Ph.D., Professor of Obstetrics and Gynecology, Northwestern University Medical School; Chief of Obstetrics and Gynecology, Passavant Memorial Hospital, Chicago; and Edwin J. DeCosta, B.S., M.D., Professor of Obstetrics and Gynecology, Northwestern University Medical School; Attending Gynecologist and Obstetrician, Passavant Memorial Hospital and Attending Gynecologist, Cook County Hospital, Chicago. The Williams and Wilkins Company, 428 East Preston St., Baltimore, Md. (21202), 1967. 918 pages, \$17.00.

A change in emphasis within the specialty of gynecology has occurred in recent years. A rapid increase in knowledge of the medical side of the specialty, especially in endocrinology and genetics, has resulted in a relative decrease in importance of the surgical aspects of the specialty. This is reflected in the fourth edition of Brewer's textbook; over 200 pages are devoted to endocrinology and genetics. Dr. DeCosta who contributed a chapter on endocrinology to the last edition is now a co-author. The remainder of the text is basically similar to early editions. An unusual format which makes this unique among textbooks of gynecology has been retained. The textbook is really two related books under one cover.

In one section, discussions of major gynecologic entities such as carcinoma of the cervix, pelvic inflammatory disease and ectopic pregnancy are arranged in the standard textbook fashion suitable for reference in conjunction with a series of didactic lectures. In the current edition, treatment of trophoblastic disease is given greater emphasis.

The other section is titled "Symptoms and Disease During Childhood, Maturity and Aging." The differential diagnosis of common presenting complaints such as uterine bleeding, leukorrhea, and dyspareunia are discussed in relation to the physical findings and age of the patient. This arrangement of material, not found in other textbooks of gynecology, is an attempt to organize the textbook material in the same manner in which the physician organizes his findings and thoughts to establish a diagnosis. This method is used regularly in teaching at the bedside and in patient-oriented seminars. This section of the book, therefore, is a learning tool which can be most effectively used during the clinical clerkship or to partially replace it. That this is the fourth edition of the text attests to its popularity with students who welcome the help it provides in synthesizing and summarizing the factual knowledge.

With this format, repetition is necessary and of definite pedagogical value. The very factors which recommend the textbook to the undergraduate student for whom it is obviously intended, however, make it somewhat less suitable as a reference source. A subject may be discussed in any one of the three sections of the book. The book is well illustrated and indexed and is a very worthwhile investment for the undergraduate student.

EMMET J. LAMB, M.D.

* * *

MANUAL OF CLOSED REDUCTION OF CLOSED FRACTURES AND DISLOCATIONS—Robert Mazet, Jr., M.D., Clinical Professor of Orthopedic Surgery, University of California at Los Angeles; Chief of the Orthopedic Service, Los Angeles Veterans Hospital; Chairman, Southern California Committee on Trauma, American College of Surgeons, Los Angeles, California. Charles C Thomas, Publisher, 301-327 East Lawrence Avenue, Springfield, Illinois (62703), 1967. 131 pages, \$10.50.

This book is a synopsis of Doctor Mazet's experience in the field of fractures. It is presented as an outline on fracture treatment but is limited in its scope as the title announces.

Surgeons, of course, differ in their favorite approaches to individual injuries. The author has attempted to pre-

sent a fair spectrum of methods for each injury, presumably stressing those which have been most successful for him. With such a personal approach, some criticism is difficult to avoid. Beginning with the opening sentence, this book is no exception.

It should be pointed out that much of the material consists of lengthy quotes from other authors (Key and Conwell, Charnley, etc.), and about half of the photographs are similarly borrowed. Doctor Mazet's contribution, then, is in organizing that which has appealed to him most and presenting it in a small book. Those from different orthopedic backgrounds may wonder at such omissions as the failure to mention traction for supracondylar humerus fractures, and may sincerely question if he really uses a carpenter's clamp to reduce metacarpal head fractures, but all must respect the vast experience from which these approaches have evolved.

The paragraphs dealing with dislocations are thorough and can be highly recommended. Conversely, the chapter on hand injuries is probably the most lacking in new techniques and principles now considered routine on many hand services.

For those interested in Doctor Mazet's philosophy and principles, this book will prove of interest. It cannot be considered as a text on fracture treatment, however, due to its unavoidable limitations.

ROBERT I. BRANNICK, M.D.

* * *

HAEMOLYTIC ANAEMIAS—Congenital & Acquired—Part III: Secondary or Symptomatic Haemolytic Anaemias—Second Edition—J. V. Dacie, M.D. (Lond.), Hon. M.D. (Uppsala), F.R.C.P. (Lond.), F.R.S., Professor of Haematology, University of London (Royal Postgraduate Medical School). Grune & Stratton, Inc., 381 Park Avenue South, New York, N. Y. (10016), 1967. 272 pages (pages 719-991), \$9.75.

This is the third book in a series of four, all devoted to the general topic of hemolytic anemia. Part III is concerned with those hemolytic anemias which are secondary to some underlying or basic disease process. The book is divided into three chapters in which the author discusses the historical and current views regarding the hemolytic anemia seen in the lymphomas, the leukemias, the myeloproliferative syndromes, the collagen diseases, liver disease, renal problems and in acute and chronic infections. Under the heading of miscellaneous conditions, Professor Dacie discusses in detail and presents a unifying concept of the newest entity in the hemolytic anemia field, micro-angiopathic hemolytic anemia. He discusses the various clinical settings in which it occurs, the pathogenesis in each, and the present concepts of therapy. The anemia seen in the uremic-hemolytic syndrome of childhood, thrombotic thrombocytopenia purpura, carcinomatosis, malignant hypertension and valvular heart disease are included in the excellent discussion. Being one of the initial investigators in this area, the author is most qualified to discuss this very interesting group of anemias which has gained much attention in the recent literature.

As Part III is a complete volume unto itself, Parts I and II are not necessarily required to appreciate the value of this particular one. The information contained in the book is mandatory for the well-rounded hematologist and oncologist and would be of great value to other clinicians. It is typical of Professor Dacie's endeavors—thoroughly complete, authoritative and concisely documented. The author easily accomplished his stated goal that "the finished book will be looked upon as a reference work of more than ephemeral value."

J. EUGENE LANG, M.D.

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KEY TO ABBREVIATIONS USED

(BRP)—Bureau of Research and Planning; (CMA)—California Medical Association; (CR)—Case Report; (Ed.)—Editorial; (I)—Information; (LE)—Letter to Editor; (MP)—Medical Progress; (MSC)—Medical Staff Conference; (N/N)—News and Notes; (Or.)—Original Article; (PE)—Page End.

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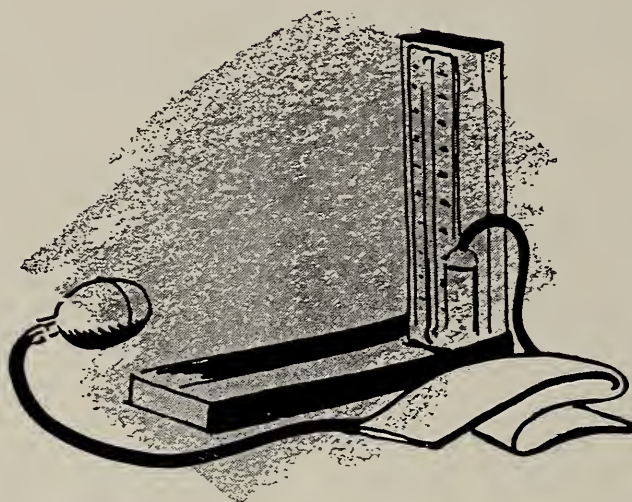
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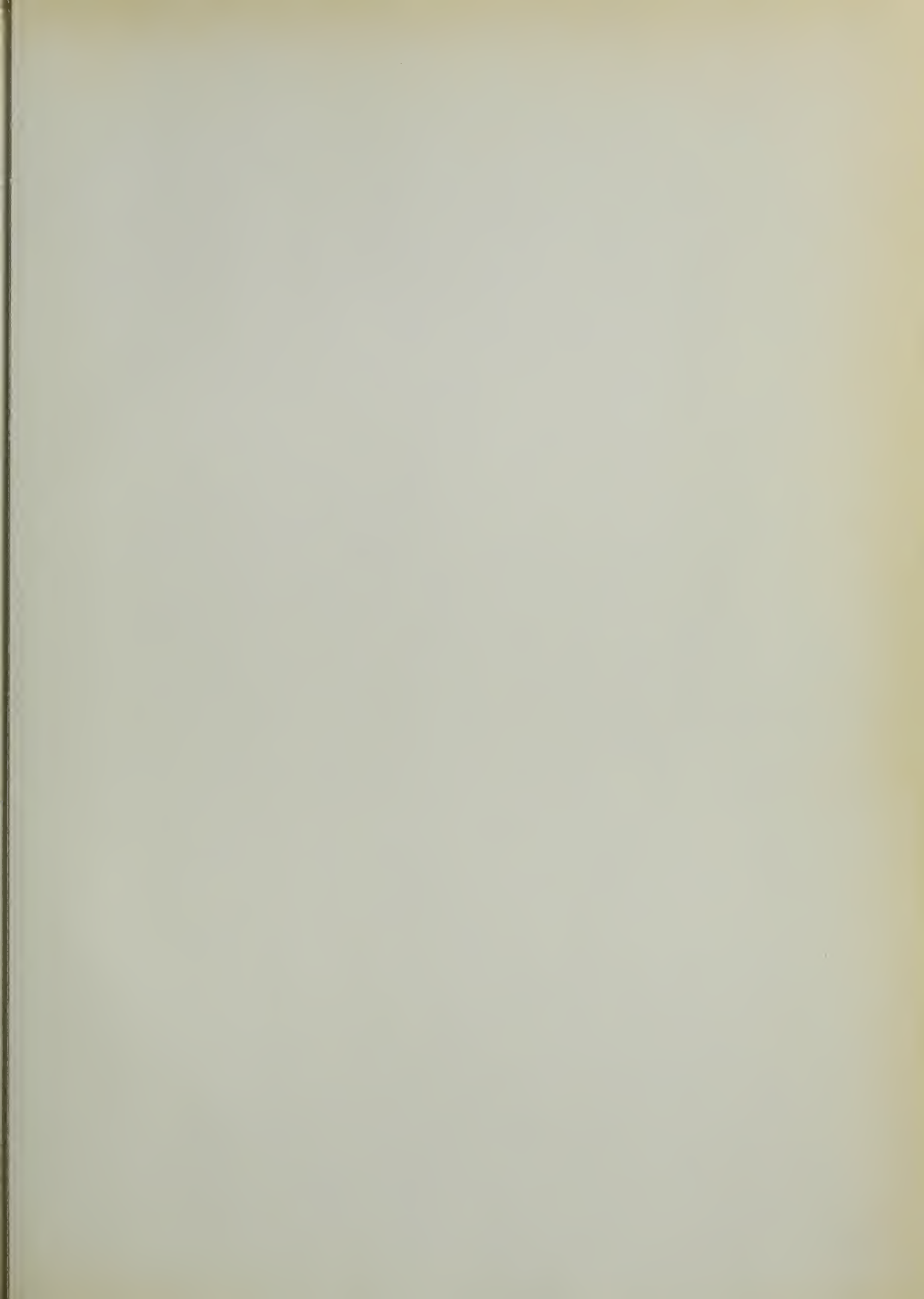
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